MORPHOLOGY, PHYSIOLOGY AND PATHOPHYSIOLOGY

CHANGES IN THE REACTIVITY OF THE VERTEBROBASILAR ARTERIES WHEN USING GLUCOSE-ELECTROLYTE DRINK WITH ANTIOXIDANT PLANT EXTRACTS DURING SUBMAXIMAL EXERCISE TEST

Tribrat N.S.[1],
Birukova E.A.[1],
Khusainov D.R.[1],
Mishin N.P.[1],
Nagaeva E.I.[1],
Burtseva E.V.[1],
Kushnir S.K.[2]

[1] V.I. Vernadsky Crimean Federal University (Vernadsky ave. 4, 295007 Simferopol, Russian Federation)
[2] Kazan State Medical University (Butlerova str. 49, Kazan 420012, Russian Federation)

Corresponding author:
Natalia S. Tribrat,
e-mail: miu-miu07@mail.ru

ABSTRACT

The aim. *To assess the effect of glucose-electrolyte composition with plant extracts having antioxidant activity on the hemodynamic parameters of vertebrobasilar system during the incrementally increasing submaximal exercise test.*

Materials and methods. *The study included 12 athletes (6 candidates for master of sports and 6 masters of sports) aged 18–22, who have been engaged in orienteering for 10 years and more. Time of aerobic exercise – 2 hours a day, five days a week. The study subjects performed an incrementally increasing submaximal exercise test and also submaximal exercise test with the preventive intake of a glucose-electrolyte composition with plant extracts having antioxidant properties.*

To assess the hemodynamic parameters in all study subjects we used Doppler ultrasound of the cerebral vessels, evaluating vertebrobasilar system blood flow, exercise gas test in the modification of hypo- and hyperventilation, and also positional test.

Results. *A single intake of glucose-electrolyte drink under conditions of incrementally increasing exercise test contributed to the manifestation of a homeostatic effect in hemodynamic parameters of the vertebrobasilar arteries. It is evidenced by the approximation to the pre-exercise level of maximum systolic velocity and average blood velocity in the breath-holding test, of the diastolic blood velocity in the hyperventilation test, and of the pulsatility index in the torsion test, as compared to the isolated submaximal exercise test which caused the change in both velocity indicators and calculated indices during the functional tests.*

The article considers the main mechanisms underlying the change in arterial hemodynamic parameters caused by incrementally increasing load, as well as describes the proposed mechanisms arising from the combined effect of an incrementally increasing load and the intake of a glucose-electrolyte composition with plant extracts having antioxidant activity.

Conclusion. *It was shown that using glucose-electrolyte drink contributed to the restoration of hemodynamic parameters of the vertebrobasilar arteries after the incrementally increasing submaximal exercise test.*

Key words: *incrementally increasing submaximal exercise test, athletes, glucose-electrolyte drink, vertebrobasilar arteries*

Received: 09.09.2022
Accepted: 12.01.2023
Published: 02.03.2023

For citation: Tribrat N.S., Biryukova E.A., Khusainov D.R., Mishin N.P., Nagaeva E.I., Burtseva E.V., Kushnir S.K. Changes in the reactivity of the vertebrobasilar arteries when using glucose-electrolyte drink with antioxidant plant extracts during submaximal exercise test. *Acta biomedica scientifica*. 2023; 8(1): 86-100. doi: 10.29413/ABS.2023-8.1.10

ИЗМЕНЕНИЕ РЕАКТИВНОСТИ АРТЕРИЙ ВЕРТЕБРОБАЗИЛЯРНОГО БАССЕЙНА ПРИ ПРИЁМЕ ГЛЮКОЗО-ЭЛЕКТРОЛИТНОГО НАПИТКА С ДОБАВЛЕНИЕМ АНТИОКСИДАНТНЫХ РАСТИТЕЛЬНЫХ ЭКСТРАКТОВ ПРИ НАГРУЗОЧНОМ ТЕСТИРОВАНИИ СУБМАКСИМАЛЬНОЙ МОЩНОСТИ

Трибрат Н.С. [1]**,**
Бирюкова Е.А. [1]**,**
Хусаинов Д.Р. [1]**,**
Мишин Н.П. [1]**,**
Нагаева Е.И. [1]**,**
Бурцева Е.В. [1]**,**
Кушнир С.К. [2]

[1] ФГАОУ ВО «Крымский федеральный университет имени В.И. Вернадского» (295007, г. Симферополь, пр. Вернадского, 4, Россия)
[2] ФГБОУ ВО «Казанский государственный медицинский университет» Минздрава России (420012, г. Казань, ул. Бутлерова, 49, Россия)

Автор, ответственный за переписку:
Трибрат Наталья Сергеевна,
e-mail: miu-miu07@mail.ru

Статья поступила: 09.09.2022
Статья принята: 12.01.2023
Статья опубликована: 02.03.2023

РЕЗЮМЕ

Цель исследования. *Оценка влияния глюкозо-электролитного состава с добавлением растительных экстрактов, обладающих антиоксидантной активностью, на гемодинамические показатели вертебробазилярного бассейна при выполнении ступенчато-возрастающей нагрузки субмаксимальной мощности.*

Материалы и методы. *В исследовании принимали участие 12 спортсменов (6 кандидатов в мастера спорта и 6 мастеров спорта) в возрасте 18–22 лет, занимающихся спортивным ориентированием в среднем 10 лет и более. Испытуемые выполняли ступенчато-возрастающую нагрузку субмаксимальной мощности, а также выполняли нагрузку субмаксимальной мощности с превентивным приёмом глюкозо-электролитного состава с добавлением растительных экстрактов, обладающих антиоксидантными свойствами. Для оценки гемодинамических показателей всем испытуемым проводили ультразвуковую допплерографию сосудов мозга, оценивая показатели кровотока в вертебробазилярном бассейне, а также нагрузочные газовые пробы – в модификации гипо- и гипервентиляции; кроме того, проводили позиционную пробу.*

Результаты. *Однократный приём глюкозо-электролитного напитка в условиях нагрузки ступенчато-возрастающей мощности способствовал проявлению гомеостатического эффекта в отношении гемодинамических показателей артерий вертебробазилярного бассейна, о чём свидетельствует приближение к уровню донагрузочных значений максимальной систолической скорости и средней скорости кровотока в пробе с задержкой дыхания, диастолической скорости кровотока – в пробе с гипервентиляцией, показателей индекса пульсации – в торсионной пробе, в отличие от изолированного выполнения нагрузки субмаксимальной мощности, после прохождения которой изменялись как скоростные показатели, так и расчётные индексы в ходе проведения функциональных проб.*

Рассмотрены основные механизмы, лежащие в основе изменения гемодинамических показателей артерий под действием ступенчато-возрастающей нагрузки, а также описаны предполагаемые механизмы, возникающие при комбинированном воздействии ступенчато-возрастающей нагрузки и приёме глюкозо-электролитного состава с добавлением растительных экстрактов, обладающих антиоксидантной активностью.

Заключение. *Показано, что приём глюкозо-электролитного напитка способствовал восстановлению гемодинамических показателей артерий вертебробазилярного бассейна после ступенчато-возрастающей нагрузки субмаксимальной мощности.*

Ключевые слова: *нагрузочное тестирование субмаксимальной мощности, спортсмены, глюкозо-электролитный напиток, артерии вертебробазилярного бассейна*

Для цитирования: Трибрат Н.С., Бирюкова Е.А., Хусаинов Д.Р., Мишин Н.П., Нагаева Е.И., Бурцева Е.В., Кушнир С.К. Изменение реактивности артерий вертебробазилярного бассейна при приёме глюкозо-электролитного напитка с добавлением антиоксидантных растительных экстрактов при нагрузочном тестировании субмаксимальной мощности. *Acta biomedica scientifica*. 2023; 8(1): 86-100. doi: 10.29413/ABS.2023-8.1.10

INTRODUCTION

Functional activity of the brain in humans is largely determined by the continuous delivery of oxygen, metabolic nutrients which are determined by the active regulation of cerebral blood flow. Therefore, maintaining proper blood flow in the brain is the most important task of the cardiovascular system, including during periods of intense physical activity, along with increasing blood flow to functioning muscles. In particular, during exercise, despite a significant increase in cardiac output up to 300–600 % [1] and blood flow in skeletal muscles up to 800 %, there is a moderate increase in blood flow in brain vessels by 10–30 %, which ensures maintenance of proper substrate delivery due to synergetic integration of the nervous, hormonal and humoral systems. According to recent studies, there is a significant heterogeneity in the response of cerebral vessels to increasing exercises and to changes in blood gas composition [2]. Moreover, it was shown that the most evident changes during intensive endurance exercise are noted to a greater extent in the vessels of the vertebrobasilar system, which is manifested as the most significant increase in perfusion in the vertebral arteries in comparison with the arteries of the carotid system [2]. The greatest sensitivity to changes in blood gas composition has also been shown for the vessels of the vertebrobasilar system by positron emission tomography (PET), according to which vasomotor reactions to hypercapnia were higher in the vertebrobasilar circulation zones than in most of the cerebral cortex supplied by the carotid system [3]. Accordingly, impaired hemodynamics of this system is accompanied by significant neurological disorders.

One of the causes of hemodynamic disorders in professional athletes is dehydration and hyponatremia occurring during prolonged (more than 40 minutes) intensive endurance training. If water and sodium requirements remain unmet, encephalopathy may develop due to overheating [4].

In milder cases, fluid volume deficit that occurs during prolonged exercise is a factor accompanying a decrease in performance. At the same time, a significant decrease in performance and endurance begins with a dehydration level of 2 % or higher [5], which is accompanied by a decrease in aerobic metabolism and, as a consequence, a deterioration in energy supply, resulting in a significant decrease in sports performance. Thus, the total loss of fluid and sodium during moderate exercise lasting more than an hour at an optimal temperature is 1 liter or more. Fluid volume deficit initiates the release of vasopressin, activation of the renin-angiotensin-aldosterone system to urgently replenish its losses. A consequence of this is an increase in blood viscosity, hypovolemia, an increase in endothelial dysfunction, an increase in cardiac rate [6].

In the study of A.N. Martinchik et al. [7] published results showing that “bottled water is the main method of rehydration in 86 % of 280 examined athletes (candidates and masters of sports). Moreover, 95–96 % of athletes in the group of martial arts and power sports use water. In other sports, there are fewer water consumers – 67–79 %. As for sports drinks, only 31 % of highly qualified endurance sports athletes and a small percentage of martial arts athletes use them only during training.”

In 2018, updated clinical recommendations of the Federal Medical and Biological Agency on methods of rehydration of the athletes’ body [7] were published, consistent with the main theses of the European Commission Scientific Committee on Food aimed at compensating daily losses during heavy muscle activity, especially in athletes [8], and their specifications. According to these clinical guidelines, drinks for athletes engaged in endurance sports should contain at least two types of sugar and should also be sodium-enriched – so-called glucose-electrolyte solutions or carbohydrate-electrolyte formulations. The content of the remaining trace elements is non-obligatory [9, 10], however, only in the case of a balanced diet of athletes [11].

It has been proven that during prolonged physical activity, solutions containing optimal sugar concentrations improve performance, increase endurance by supplying working muscles with carbohydrates and preventing depletion of glycogen reserves, maintaining the oxygen balance in the blood with the help of antioxidants [12].

Currently, sports drinks in a wide range are presented mainly by foreign manufacturers. Domestic goods are represented by few items. For nutrient enrichment, endurance growth and training effectiveness, herbal extracts with antioxidant properties are often added to sports drinks, although the effect of the latter on the functioning of muscle tissue under high exercise activity is currently a debatable issue [13]; however, the role of antioxidants for the cardiovascular system, including under sports exercises, has high evidence-based potential [14].

At the same time, given the biodiversity of vegetation, the developed essential oil production in the Republic of Crimea, as well as the developed sports sector (orienteering, sports tourism), it is proposed to improve the basic formulation of glucose-electrolyte composition by adding aqueous extracts of rosehip fruit, nettle leaf, lemon juice, as well as rosemary hydrolate, which have strong antioxidant properties, and enrichment with vitamin and mineral premix that helps nutrient enrich athletes.

Accordingly, **the aim of this study** was to assess the effect of glucose-electrolyte composition with antioxidant plant extracts, based on plant raw materials produced in ecologically clean regions of the Republic of Crimea, on the blood flow indicators of the vertebrobasilar system during the incrementally increasing submaximal exercise test.

MATERIALS AND METHODS

The study was carried out at the Center for the Collective Use of Scientific Equipment “Experimental Physiology and Biophysics” of the V.I. Vernadsky Crimean Federal University.

The study involved 12 athletes (6 candidates for masters of sports and 6 masters of sports) aged 18–22 years engaged in orienteering. The experience of sports exercises averaged 10 years or more. Aerobic exercise mode – 2 hours a day for five days a week.

To assess hemodynamic parameters, all subjects underwent ultrasound dopplerography (USDG) of vessels, assessing blood flow in the vertebrobasilar system (symmetrical vertebral arteries and the basilar artery), as well as gas stress tests – in the modification of hypo- and hyperventilation; in addition, a positional test was performed. USDG of brain vessels was performed on Sonomed 300 (Nizhny Novgorod).

To assess the effect of glucose-electrolyte composition on the hemodynamic parameters of the vertebrobasilar system, two study cycles were conducted:

1. The first cycle of the study included velocity indicators recording, as well as calculated indices of USDG along the arteries of the vertebrobasilar system. In addition, in the first cycle of the study, functional tests were carried out, including hyper- and hypoventilation tests with simultaneous registration of USDG indicators along the basilar artery and positional tests of symmetrical vertebral arteries, also with simultaneous registration of USDG indicators.

During the study, the following indicators of blood flow along the basilar and vertebral arteries (symmetrical) were assessed:

V_{max} – maximum systolic blood flow velocity;

V_{min} – diastolic blood flow velocity;

V_{aver} – average blood flow velocity;

Ri – Pourcelot's resistance index, which reflects the state of resistance to blood flow distal to the measurement site and is the ratio of the difference between the maximum systolic and end diastolic velocities to the maximum systolic velocity:

$$Ri = \frac{\left(V_{max} - V_{min}\right)}{V_{max}};$$

Pi – pulsatility index (also known as the Gosling index), which reflects the elastic properties of the arteries, decreases with age and represents the ratio of the difference between the maximum systolic and diastolic velocities to the average velocity:

$$Pi = \frac{\left(V_{max} - V_{min}\right)}{V_{aver}}.$$

Additionally, ventilation tests were performed to assess the state of the metabolic circuit of cerebral blood flow regulation by locating the basilar artery.

Before conducting a breath-holding test, the subject was warned about the need to exhale on signal and hold his/her breath for the maximum possible period. Hemodynamic parameters were recorded during the period of breath holding at the time of a steady change of velocity indicators, after which the subject could inhale and resume the usual breathing rhythm.

The hyperventilation test was started after a complete stable recovery of the USDG pattern. When performing a hyperventilation test, the subject began forced breathing. Monitoring of the hyperventilation tests was started from the moment of intensive breathing, waiting for the moment when the amplitude of the spectral signals would stop changing; the last 5–6 complexes were recorded on the screen, after which the subject resumed the usual breathing rhythm.

After complete restoration of the USDG pattern, a positional (torsion) test was performed along the vertebral arteries on both sides sequentially. During the positional test, the subject performed a slow turn of the head and neck away from the sensor, achieving maximum amplitude (chin to shoulder), lowering his/her head so as to reach the level of the shoulder joint with his/her nose.

After the background (baseline) study of USDG, the subjects were offered 250 ml of bottled water with the addition of a flavoring agent imitating the aroma of the drink under study.

After the USDG and intake of bottled water, the athletes were offered an exercise test, including an incrementally increasing load on the Kettler bicycle ergometer (KETTLER Holding GmbH, Germany) from the starting position of 50 Watts followed by an increase by 50 Watts every 3 min of the exercise stage. The exercise test was completed at the request of the athlete – "up to failure".

As soon as the athletes performed the submaximal exercise test, USDG values of the vertebrobasilar arteries were recorded again, taking into account the performance of functional tests.

2. The second cycle was carried out two weeks after the first one. The second cycle was methodically similar to the first one, with the difference that in the second cycle, as a replenishment of fluid and electrolytes, athletes were offered a glucose-electrolyte composition with the addition of plant extracts with antioxidant properties in the amount of 250 ml 15 min before the exercise test. The athletes were stopped at the same exercise stage at which they completed the exercise in the first cycle.

Glucose-electrolyte solution composition includes a natural mineral complex in the form of sea salt of the Black Sea obtained by natural evaporation in the waters of Sasyk-Sivash Lake – 0.4 g; prepared drinking water – up to the required volume, rosemary hydrolate (aromatic water) – 65 ml; water extract of rosehip fruits (1:10) – 100 ml; water extract of nettle leaf (1:10) – 100 ml; maltodextrin, glucose, lemon juice – 5 ml; ascorbic acid, potassium sorbate, sodium benzoate. Glucose-electrolyte drink complies with TR CU 022/2011, standardized according to GOST R 56543-2015 (Table 1).

The subjects who took part in the study did not have any chronic cardiovascular or respiratory pathology. None of the athletes took drugs that affect vascular tone. On the day of the study, the subjects did not undergo any preliminary physical activities. The study was conducted in the morning (10^{00}–13^{00}).

All procedures performed in human studies comply with the ethical standards of the National Committee for Ethics in Research and the Declaration of Helsinki (1964) and its subsequent revisions or comparable ethical standards. Informed voluntary consent was obtained from each of the participants included in the study. Minutes of the meeting of the Ethics Committee of V.I. Vernadsky Crimean Federal University No. 1 dated January 25, 2022.

TABLE 1

ENERGY VALUE AND CHEMICOANALYTICAL COMPOSITION OF THE DRINK

Indicator	Content	
	in 100 ml	in 250 ml
Carbohydrates (g), incl.	8.0	20.0
glucose, g	2.0	5.0
maltodextrin, g	6.0	15.0
Ascorbic acid, g	0.2	0.5
Sodium, mg	37.6	94.0
Calcium, mg	1.6	4.0
Potassium, mg	21.2	53.0
Chlorides, mg	84.0	210.0
Essential oil, g	0.016	0.04
Energy value, kcal/kJ	23/97	58/241

The Shapiro – Wilk test was used to check the distribution of the data array for normality, and the results showed that the data array did not follow a normal distribution. In this regard, the Friedman non-parametric test was used to determine the statistical significance of differences in the linked sample when comparing three arrays. In the case of pairwise comparison of linked samples, the Wilcoxon test was used. For clarity of description and visualization of the results obtained, the average values were used, as well as the error of the mean.

Calculations and graphic design of the data obtained in this paper were carried out using Microsoft Excel (Microsoft Corp., USA) and Statistica 8.0 software package (StatSoft Inc., USA).

STUDY RESULTS

As the results of the first and second study cycles showed, the main differences in the USDG indicators, recorded after the incrementally increasing submaximal exercise test, were only available in relation to the data recorded during the functional tests in comparison with the level of pre-exercise values of the corresponding indicators.

The values of hemodynamic parameters of the vertebrobasilar arteries registered outside the functional tests after the incrementally increasing submaximal exercise test were close to the baseline values (Table 2). Such stability of blood flow velocity indicators indicates a high degree of fitness and endurance during aerobic exercises and, as a result, a high degree of synchronization and stability of both the cardiorespiratory system and the musculoskeletal system during incrementally increasing aerobic exercise.

The results of the first study cycle, when athletes performed only an incrementally increasing submaximal exercise test, indicate changes in a number of velocity indicators and calculated indices, recorded during functional tests after incrementally increasing load, in comparison with the level of pre-exercise data of the corresponding indicators, recorded during similar tests (Table 3).

The results of the second study cycle, when athletes took a glucose-electrolyte drink followed by submaximal exercise, indicate the stability of the hemodynamic parameters of the investigated arteries, since the values of the studied indicators obtained after exercises and taking a glucose-electrolyte drink were close to the baseline values (Table 3).

In particular, the results of the first cycle study indicate that the performance of the incrementally increasing submaximal exercise test is accompanied by an increase in the V_{max} index by 21.07 % ($p < 0.05$) during the period of the breath-holding test in the basilar artery relative to the data of this indicator registered in the pre-exercise period during a similar test.

The results of the second cycle study indicate that performing submaximal exercise test and taking a glucose-electrolyte drink prevent changes in the values of the V_{max} index in comparison with the level of pre-exercise values of this indicator in the breath-holding test.

A comparative analysis of the results of the first and second study cycles indicates that the V_{max} index was lower by 14.57 % ($p < 0.05$) in the case of glucose-electrolyte drink intake and exercise relative to the data of this indicator recorded during isolated exercise test during the breath-holding test, and approached the level of pre-exercise values.

Thus, glucose-electrolyte drink intake prevented changes in the V_{max} index when performing submaximal exercise test during the breath-holding test.

Similarly, the dynamics of the V_{aver} indicator changed during the breath-holding test. Thus, the performance of incrementally increasing exercise test in the first cycle was accompanied by an increase in this indicator by 24.58 %

TABLE 2

DYNAMICS OF PARAMETERS OF DOPPLER ULTRASOUND OF VERTEBROBASILAR ARTERIES IN PROFESSIONAL ORIENTEERS, REGISTERED BEFORE AND AFTER INCREMENTALLY INCREASING LOAD, AS WELL AS BEFORE AND AFTER INCREMENTALLY INCREASING LOAD IN COMBINATION WITH TAKING A GLUCOSE-ELECTROLYTE DRINK

Study phases	The arteries under study	USDG indicators of vertebrobasilar arteries				
		V_{max}, cm/s	V_{min}, cm/s	V_{aver}, cm/s	Ri	Pi
Background (cycle I)	BA	70.09 ± 4.06	32.74 ± 1.38	42.15 ± 1.66	0.53 ± 0.01	0.88 ± 0.06
	VA on the right	57.62 ± 2.73	27.09 ± 2.57	36.26 ± 2.19	0.52 ± 0.04	1.04 ± 0.28
	VA on the left	51.78 ± 6.79	30.73 ± 4.88	38.03 ± 5.39	0.45 ± 0.03	0.68 ± 0.08
Exercise (cycle I)	BA	73.56 ± 6.96	35.7 ± 3.63	46.8 ± 4.32	0.51 ± 0.02	0.83 ± 0.10
	VA on the right	52.8 ± 5.86	30 ± 3.17	35.8 ± 5.87	0.43 ± 0.21	0.67 ± 0.10
	VA on the left	52.8 ± 5.97	27.2 ± 5.83	35.6 ± 6.13	0.48 ± 0.08	0.77 ± 0.21
Background (cycle II)	BA	70.16 ± 3.78	33.10 ± 1.18	43.78 ± 2.85	0.52 ± 0.02	0.89 ± 0.06
	VA on the right	53.02 ± 4.01	28.80 ± 2.01	37.05 ± 2.95	0.53 ± 0.03	1.01 ± 0.07
	VA on the left	52.50 ± 3.28	30.54 ± 2.59	36.15 ± 2.14	0.48 ± 0.02	0.65 ± 0.04
Glucose-electrolyte composition + exercise (cycle II)	BA	65.6 ± 3.97	30.35 ± 1.8	37.95 ± 1.27	0.53 ± 0.03	0.92 ± 0.08
	VA on the right	67.51 ± 5.32	33.34 ± 3.54	40.78 ± 3.21	0.48 ± 0.03	0.81 ± 0.11
	VA on the left	50.45 ± 4.27	27.67 ± 2.27	32.65 ± 2.09	0.44 ± 0.03	0.69 ± 0.07

Note. BA – basilar artery; VA – vertebral artery.

($p < 0.05$) relative to the data of this indicator recorded before submaximal exercise (Fig. 1).

The intake of glucose-electrolyte composition and subsequent incrementally increasing exercise test did not significantly change the values of this indicator in comparison with the level of pre-exercise values recorded in the breath-holding test.

A comparative analysis of the results of cycles I and II of the study shows a decrease in the V_{aver} index by 18.37 % ($p < 0.05$) after submaximal exercise test in combination with the intake of glucose-electrolyte composition in comparison with the data of this indicator obtained after the isolated submaximal exercise test, and an approximation of V_{aver} index values in cycle II to the level of pre-exercise values obtained during the breath-holding test.

Thus, taking a glucose-electrolyte drink prevented changes in V_{max} and V_{aver} indices after the submaximal exercise test, and the results of the incrementally increasing exercise test after the tested drink intake are comparable with baseline data recorded in the pre-exercise period during the breath-holding test.

V_{min} had similar dynamics of change as the V_{max} and V_{aver} indices, but without achieving a statistically significant difference.

During the hyperventilation test, there were also changes in velocity indicators along the basilar artery.

The results of the hyperventilation test showed similar, but not identical results.

Thus, V_{min} increased by 25.87 % ($p < 0.05$) after the isolated incrementally increasing exercise test relative to base-

TABLE 3

DYNAMICS OF PARAMETERS OF DOPPLER ULTRASOUND OF VERTEBROBASILAR ARTERIES OF PROFESSIONAL ORIENTEERS DURING FUNCTIONAL TESTS REGISTERED BEFORE AND AFTER INCREMENTALLY INCREASING LOAD (CYCLE I), AS WELL AS BEFORE AND AFTER INCREMENTALLY INCREASING LOAD IN COMBINATION WITH TAKING A GLUCOSE-ELECTROLYTE DRINK

Study phases	The arteries under study	USDG indicators of vertebrobasilar arteries				
		V_{max}, cm/s	V_{min}, cm/s	V_{aver}, cm/s	Ri	Pi
Background (cycle I)	BA (hyperventilation)	61.25 ± 3.05	28.92 ± 1.54	36.71 ± 1.83	0.52 ± 0.01	0.87 ± 0.05
	BA (breath holding)	64.39 ± 3.27	32.17 ± 1.93	40.79 ± 2.28	0.49 ± 0.02	0.80 ± 0.07
	VA (torsion) on the right	50.50 ± 3.74	24.77 ± 1.13	33.48 ± 1.41	0.49 ± 0.02	0.74 ± 0.05
	VA (torsion) on the left	43.42 ± 2.9	25.26 ± 1.43	28.03 ± 1.61	0.51 ± 0.04	0.80 ± 0.07
Exercise (cycle I)	BA (hyperventilation)	73.93 ± 1.61 $p < 0.05$	35.61 ± 2.56 $p < 0.05$	43.90 ± 3.19	0.51 ± 0.04	0.90 ± 0.15
	BA (breath holding)	77.96 ± 7.81 $p < 0.05$	40.82 ± 5.36	50.82 ± 4.83 $p < 0.05$	0.47 ± 0.04	0.75 ± 0.13
	VA (torsion) on the right	49.06 ± 7.01	28.53 ± 3.40	36.8 ± 4.29	0.41 ± 0.01	0.54 ± 0.03 $p < 0.05$
	VA (torsion) on the left	39 ± 10.42	20 ± 2.01	19.8 ± 3.32	0.42 ± 0.11	0.45 ± 0.14 $p < 0.05$
Background (cycle II)	BA (hyperventilation)	61.38 ± 3.48	28.36 ± 1.28	37.01 ± 1.45	0.53 ± 0.02	0.87 ± 0.04
	BA (breath holding)	64.24 ± 2.47	31.79 ± 1.32	40.21 ± 2.16	0.46 ± 0.03	0.81 ± 0.04
	VA (torsion) on the right	51.29 ± 2.99	24.17 ± 1.73	34.67 ± 1.31	0.48 ± 0.01	0.75 ± 0.04
	VA (torsion) on the left	44.12 ± 2.91	25.71 ± 1.92	27.05 ± 1.72	0.53 ± 0.03	0.80 ± 0.06
Glucose-electrolyte drink + exercise (cycle II)	BA (hyperventilation)	72.8 ± 6.35 $p < 0.05$	30.62 ± 2.88 $p_1 < 0.05$	37.82 ± 2.41 $p_1 < 0.05$	0.56 ± 0.03	1.12 ± 0.14 $p < 0.05$
	BA (breath holding)	66.60 ± 3.65 $p_1<0.05$	33.77 ± 1.99	41.48 ± 1.44 $p < 0.05$	0.49 ± 0.01	0.79 ± 0.04
	VA (torsion) on the right	55.61 ± 4.10	27.24 ± 1.87	34.12 ± 1.97	0.50 ± 0.03	0.83 ± 0.11 $p_1 < 0.05$
	VA (torsion) on the left	54.8 ± 6.01	29.52 ± 3.95	32.41 ± 4.35	0.46 ± 0.03	0.83 ± 0.1 $p_1 < 0.051$

Note. $p < 0.05$ is statistical significance of the differences according to the Wilcoxon test when comparing baseline values and values obtained during exercise test in cycle I, and statistical significance of the differences obtained when comparing baseline values and values obtained after taking glucose-electrolyte drink followed by an incrementally increasing load in cycle II; $p_1 < 0.05$ is statistical significance of the differences according to the Friedman test when comparing background values and values obtained after performing isolated exercise test and exercise in combination with glucose-electrolyte drink.

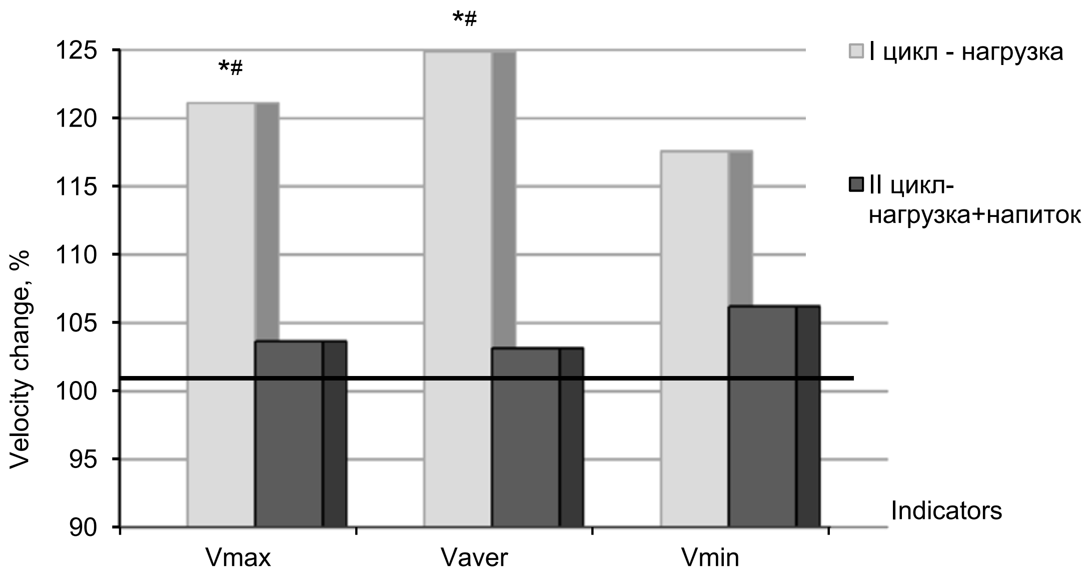

FIG. 1.
*The changes in the velocity indicators of the basilar artery during breath-holding test before and after an incrementally increasing load (cycle I), as well as before and after an intake of the glucose-electrolyte drink followed by an incrementally increasing load (cycle II), in percent relative to the values recorded before the load (taken as 100 %): * – statistical significance of differences according to the Wilcoxon between background values and values obtained during exercise test in the cycle I, and between background values and values obtained after the combination of an intake of the glucose-electrolyte drink with exercise in the cycle II ($p < 0.05$); # – statistical significance of differences according to the Friedman test between background values and values obtained after an isolated exercise test and after the combination of an intake of the glucose-electrolyte drink with exercise ($p_1 < 0.05$)*

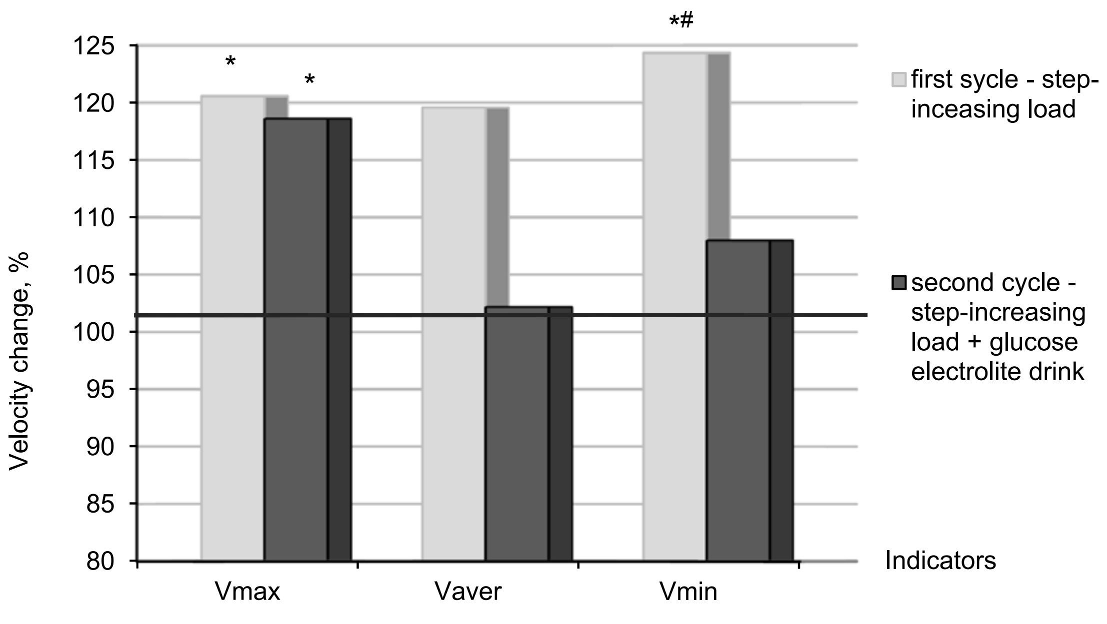

FIG. 2.
*The changes in the velocity indicators of the basilar artery during hyperventilation test before and after an incrementally increasing load (cycle I), as well as before and after an intake of the glucose-electrolyte drink followed by an incrementally increasing load (cycle II), in percent relative to the values recorded before the load (taken as 100 %): * – statistical significance of differences according to the Wilcoxon between background values and values obtained during exercise test in the cycle I, and between background values and values obtained after the combination of an intake of the glucose-electrolyte drink with exercise in the cycle II ($p < 0.05$); # – statistical significance of differences according to the Friedman test between background values and values obtained after an isolated exercise test and after the combination of an intake of the glucose-electrolyte drink with exercise ($p_1 < 0.05$)*

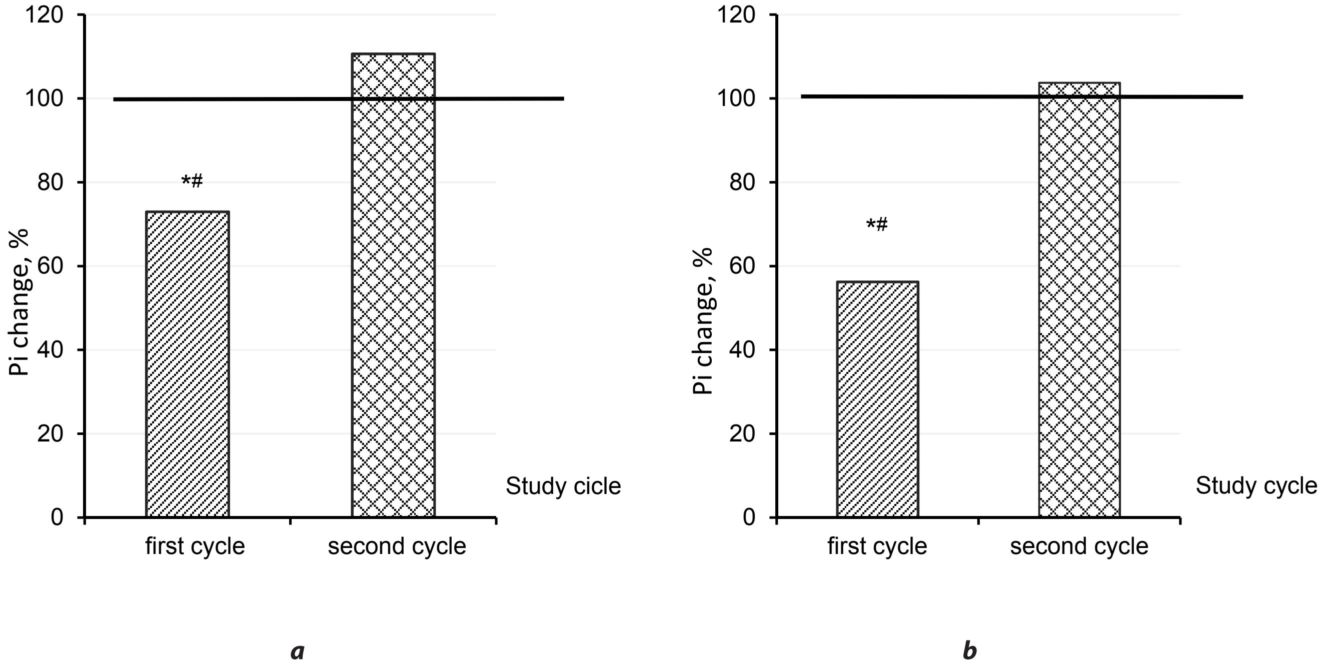

FIG. 3.

*The changes in the Gosling index (Pi) on the vertebral artery right (a) and left (b) during the torsion test before and after an incrementally increasing load (cycle I), as well as before and after an intake of the glucose-electrolyte drink followed by an incrementally increasing load (cycle II), in percent relative to the values recorded before the load (taken as 100 %): * – statistical significance of differences according to the Wilcoxon between background values and values obtained during exercise test in the cycle I, and between background values and values obtained after the combination of an intake of the glucose-electrolyte drink with exercise in the cycle II ($p < 0.05$); # – statistical significance of differences according to the Friedman test between background values and values obtained after an isolated exercise test and after the combination of an intake of the glucose-electrolyte drink with exercise ($p_1 < 0.05$)*

line data of this indicator recorded during the hyperventilation test (Fig. 2).

Glucose-electrolyte drink intake and subsequent incrementally increasing exercise test did not statistically significantly change the V_{min} value during the hyperventilation test.

A comparative analysis of the results of the first and second study cycles shows a 14.01 % ($p < 0.05$) decrease of V_{min} index in cycle II after exercise and drink intake in comparison with the values of this indicator recorded in cycle I after an isolated exercise test during the hyperventilation test (Fig. 2). Thus, the intake of the drink under study followed by exercise prevented changes in the V_{min} index in the hyperventilation test.

A slightly different dynamics characterized the V_{max} index during the hyperventilation test. Thus, V_{max} increased after isolated exercise test by 19.32 % ($p < 0.05$) relative to baseline data for this indicator.

Glucose-electrolyte drink intake and subsequent incrementally increasing exercise test were also accompanied by an increase in this indicator by 18.61 % ($p < 0.05$) in comparison with its baseline data recorded during the hyperventilation test (Fig. 2).

There was no difference in V_{max} during the hyperventilation test after exercise in cycles I and II.

Consequently, glucose-electrolyte drink intake did not prevent the change in V_{max} during the hyperventilation test.

During the positional (torsion) test assessing extravasal influences, stability in relation to most velocity indicators to the athletes' performance of a submaximal exercise test was noted along the vertebral arteries. Changes after an isolated exercise test and exercise in combination with taking a glucose-electrolyte drink were noted only according to the Gosling index data.

Thus, when registering a torsion test along the vertebral artery on the right side, performing incrementally increasing exercise test led to a one-third decrease in the Gosling index ($p < 0.05$) relative to the values of this indicator recorded in the pre-exercise period during the torsion test.

Taking glucose-electrolyte drink in combination with submaximal exercise test contributed to the inversion of the response – a tendency to increase this indicator to values of 0.84 ($p < 0.05$) (Fig. 3a), comparable with its baseline values.

Differences in Pi registered after performing an isolated exercise test and performing exercise in combination with taking glucose-electrolyte composition reached values of 53 % ($p < 0.05$). It is worth noting that the values of this indicator registered in cycle II were close to the pre-exercise level in comparison with the values obtained in cycle I of the study (Fig. 3a).

Similar dynamics of the Gosling index were recorded during a torsion test along the vertebral artery on the left side. Isolated exercise test contributed to a 43.75 % ($p < 0.05$) decrease in Pi in comparison with the pre-exercise period during the test (see Fig. 3b).

The values of the Gosling index after taking a glucose-electrolyte drink and performing submaximal exercise test practically were practically unchanged in cycle II of the study and corresponded to the level of pre-exercise values.

The resulting differences in the Gosling index values after exercise for cycles I and II of the study were over 50 % ($p < 0.05$) (see Fig. 3b).

Thus, a single intake of a glucose-electrolyte drink followed by exercise contributed to the manifestation of a homeostatic effect with respect to the mechanisms of regulation of arterial hemodynamics in the vertebrobasilar system under incrementally increasing submaximal exercise test conditions, as evidenced by the stability of most hemodynamic parameters recorded after taking the drink and performing incrementally increasing exercise test, as opposed to an isolated submaximal exercise test after passing which both velocity parameters and calculated indices changed during functional tests.

RESULTS DISCUSSION

During the period of intense physical activity, taking into account the high energy consumption of the brain and the absence of significant intracellular energy reserves, accurate control of the intake of nutrients and byproducts is supported by changes in cerebral circulation, which is coordinated by the operation of various regulatory mechanisms. If the mechanisms of regulation of vascular tone at rest are well known, then during the period of active physical activity they have not yet been fully determined. Basal vascular tone, vegetative innervation and regional heterogeneity in ion channels or NO production play a significant role. However, the greatest contribution to the regulation of cerebral blood flow during aerobic exercise is made by changes in arterial blood gas content, metabolic changes, arterial pressure, cardiac output, neurovascular innervation, as well as endothelial reactivity [15]. The separation of these contributions is highly problematic due to the redundancy of the cardiovascular system to achieve complex regulation, which has led to discrepancies in the definition of key participants in the regulation of blood flow during exercise [15].

As it was shown in this study, submaximal exercise and subsequent breath-holding test were accompanied by a marked increase in both systolic and average velocity values in comparison with the data of the corresponding indicators recorded before performing submaximal exercise in the course of a similar test.

The increase in velocity indicators during the breath-holding test is a response to an increase in partial pressure of CO_2, which is accompanied by an increase in the H^+ level, resulting in an increase in the osmolarity level and the subsequent dilation reaction. However, performing a submaximal exercise followed by a breath-holding test is accompanied by a large decrease in pH due to lactate accumulation, which may be accompanied by changes in cerebral hemodynamics and an increase in blood flow, on the one hand. This was probably the reason for the increase in velocity indicators along the basilar artery after submaximal exercise in the period of the breath-holding test in comparison with the data during a similar test before submaximal exercise.

On the other hand, blood flow is linearly dependent on cardiac output, which increases in proportion to exercise [16]. At the same time, contrary to the recently prevailing views about the constancy of cerebral hemodynamics under any conditions, including when performing physical activity, according to the studies of recent years, the response of cerebral blood flow to prolonged aerobic exercise is described as biphasic, with a distinct progressive increase, respectively increasing exercise intensity to approximately 60 % of maximum consumption oxygen with subsequent access to the plateau [15]. Probably, the increase in V_{max}, depending on cardiac output, after submaximal exercise during the breath-holding test can be explained both by an increase in cardiac output and a more intense decrease in the pH level.

Hyperventilation test after submaximal exercise was accompanied by an increase in the V_{min} index, which indicates a decrease in peripheral resistance of resistive vessels and probably dictated by metabolic changes, namely a moderate drop in pH due to lactate accumulation relative to the data of this indicator recorded before the athletes performed exercises during a similar test.

In addition, as per the results of the torsion test, after the athletes performed submaximal exercise test, there was a decrease in the Gosling index, depending on the elasticity of the vascular wall. Arterial elasticity, in turn, is determined by both structural elements and tone of vascular smooth muscles. And if the first group of factors is more stable, then the second depends largely on the level of functional activity of the vascular endothelium due to the significant representation of receptors to a huge number of humoral factors on its surface and the ability to release both constrictors and dilators in response.

There are studies indicating endothelial dysfunction in professional athletes engaged in endurance sports [17].

The supposed mechanism of endothelial dysfunction in athletes lies in the avalanche-like production of reactive oxygen species that oxidize low-density lipoprotein molecules with the formation of oxidized low-density lipoprotein (oxLDL) [18], whose high content in the bloodstream is toxic to endotheliocytes, since oxLDL can induce necrosis and apoptosis of endothelial cells. In this case, oxLDL lead to activation of immunocompetent cells accompanied by autosensitization and accumulation of autoantibodies in blood. Antibodies, forming immune complexes with oxLDL, have an additional damaging effect on the endothelium. In this regard, the endothelium reactionary activity, which is actively involved in adaptive reactions to physical activity, changes. And if, normally, the balance of functional activity of the endothelium shifts towards the release of vasodilators, anti-inflammatory, and antithrombic factors, then when the endothelium is attacked by immune complexes with oxLDL – towards the release of vasoconstrictors, as well as prothrombic and proinflammatory factors. This is supported by experimental data that among skiers, athletes engaged in rowing, as well as cycling, signs of early atherosclerosis and a tendency to thrombosis were detected in 60.5 % of cases [19]. A study by Z.V. Lopatin and V.S. Vasilenko [20] showed an increase in the level of homocysteine up to 18 mmol/L and D-dimer in professional athletes engaged in endurance sports. Moreover, hyperhomocysteinemia is determined at the plasma concentration of 10 μmol/L and higher and is associated with the development of cardiovascular diseases due to endothelial dysfunction development and contributes to an increase in the risk of acute cerebral circulation disorders of both ischemic and hemorrhagic types due to promotion of atherogenesis and atherothrombosis of cerebral vessels, increased activity of matrix metalloproteinases [21].

At the same time, oxidative stress caused by homocysteinemia significantly reduces the bioavailability of nitric oxide and leads to the dysregulation of intracellular signaling and gene expression.

During intensive athletes' training, there is an increase in systolic pressure, which entails constant changes in shear stress and stimulates the production of not only nitric oxide, but also free oxygen forms. In the chronic mode, such changes cause endothelial overstimulation effect, as well as maladaptation [22].

It is possible to assume that a glucose-electrolyte drink with antioxidant plant extracts behaves similarly to the adaptogens of natural origin, although it does not belong to the classical representatives of this kind, since the leading components in the composition of the drink under study are rosemary hydrolate, lemon juice, nettle leaf, rosehip fruit vitamin premix, as well as trace elements. Traditionally, natural adaptogens are ginseng, rhodiola rosea, *Schisandra chinensis* (lemongrass), Eleutherococcus, leuzea, and arabia. It is these adaptogens that have a large evidence base, including in relation to sports achievements [13]. A number of substances that make up the plant extracts (on the basis of which the drink under study was made) are also part of traditional adaptogens, probably in lower concentrations, and in combination with other substances. Probably, the tested glucose-electrolyte composition with antioxidant plant extracts affects various links of regulatory mechanisms that control hemodynamics of the studied vessels.

Thus, during the incrementally increasing submaximal exercise test, it is natural to overload the electron transport chain in the mitochondrial membranes, which results in the production of an excessive number of free radicals that damage mitochondrial membranes, which leads to a decrease in cell energy. In this respect, a single intake of a glucose-electrolyte drink with antioxidant plant extracts, including lemon juice, as well as nettle and rosehip extract, due to which high ascorbic acid content is achieved, has an effect on changing energy processes in cells. In addition, the composition of rosehip and traditional adaptogens, such as rhodiola rosea and Schisandra chinensis (lemongrass), combine organic acids, represented mainly by citric, succinic and malic. The content of organic acids, especially citric and succinic in combination with ascorbic acid significantly intensifies the activity of the Krebs cycle. Besides, ascorbic acid, being involved in the biochemical processes of inhibiting free-radical reactions, probably contributes to a decrease in the activity of lipid peroxidation processes [23].

Rosemary hydrolate containing rosmarinic acid helps tissues to better utilize glucose [24]. In a study by M. Prasannarong et al. [25] it was shown that even a single dose of rosmarinic acid at a dose of 10 mg/kg helped to reduce angiotensin II effects and improved glucose transport to the skeletal muscles.

The fructose solution, which is part of the glucose-electrolyte composition, is a donor of the nutrient substrate.

In addition, nettle extract, as has been shown in recent studies, in combination with endurance exercise improves the functioning of mitochondria, as well as the expression of nuclear respiratory factor 2 of the heart muscle and gamma coactivator 1-alpha [26].

Accordingly, the intake of the investigated drink containing fructose solution in combination with rosmarinic acid, lemon juice, nettle and rosehip extracts forms a chain of reactions, on the one hand, supplying the substrate, ensuring its high utilization and effective oxidation, and on the other hand, the intake of glucose-electrolyte composition shifts the pH level to the alkaline side. It is likely that a moderate increase in pH after taking the glucose-electrolyte composition, as well as activation of energy processes, contributed to the restoration of autoregulation, which probably stabilized the V_{max} and V_{aver} velocity indicators during the breath-holding test after submaximal exercise test (see Fig. 1).

A single consumption of the studied glucose-electrolyte drink by athletes and the subsequent performance of the incrementally increasing submaximal exercise test also helped to prevent the increase in V_{min} observed after the isolated exercise during the hyperventilation test. The stabilization of this indicator after taking the tested drink and exercise indicates restoration of arterial tone, probably due to the effect of flavonoids such as rutin, quercetin, heperedin, toning the vascular wall, which are part of rosehip in the studied drink. The same substances are part of traditional adaptogens, such as *Rhodiola rosea* and *Leuzea*.

Taking a glucose-electrolyte drink did not affect the dynamics of V_{max} in the hyperventilation test after the first and second cycles. The absence of other distinct changes in professional athletes during the hyperventilation test within the first and second cycles of the study may indicate that oxygenation appears to be a fairly strong regulatory factor [16], in comparison with other metabolic and humoral factors.

In addition, the intake of glucose-electrolyte composition contributed to the stabilization of the Gosling index (pulsatility index) after submaximal exercise, whereas isolated exercise performance contributed to its significant drop. Given the dependence of this indicator on the elasticity of the vascular wall, which in turn is mostly determined by vascular endothelium functional activity, it can be assumed that the effect of taking the glucose-electrolyte drink was induced by substances in its composition, in particular, by polyphenolic compounds contained in the lemon juice, rosemary hydrolate, and rosehip extract.

It is known that flavonoids contained in rosehips, such as hesperidin, quercetin, rutin, have high antioxidant, anti-inflammatory activity, and also have a high tropism to the vascular system [27], in particular to the vascular endothelium, changing its apoptosis pathways [28], promoting nitric oxide increase, improving its responsiveness to influencing factors by modulating endothelium-dependent vasodilation [29]. Intake of products containing polyphenolic compounds, in particular bioflavonoids, affects the following mechanisms of endothelium-dependent vasodilation: an increase in the level of Ca^{2+} and redox activation of the phosphoinositide-3 (PI3) kinase/Akt pathway are noted in endotheliocytes, leading to rapid and sustained activation of nitric oxide synthase (NOS) [30], as well as the formation of an endothelium-dependent hyperpolarization factor. In addition to the described long-term effects of flavonoids, short-term effects are also known, including NO-mediated vasorelaxation due to an increase in the influx of extracellular Ca^{2+} and mobilization of intracellular Ca^{2+} in endothelial cells. This is supported by evidence that an increase in endothelium-dependent vasodilation is observed even after a single intake of ascorbic acid [30].

CONCLUSION

Thus, the isolated performance of the incrementally increasing submaximal exercise test contributes to changes in velocity indicators and calculated indices of the vertebrobasilar arteries during functional tests performance with breath-holding, hyperventilation, as well as a torsion test, which indicates the development of tension regulation of cerebral blood flow in the conditions of the studied load regime. A single intake of glucose-electrolyte composition with antioxidant plant extracts contributes to stabilization of hemodynamic parameters of the vertebrobasilar arteries under incrementally increasing submaximal exercise test conditions, preventing changes in parameters observed after isolated exercise. Thus, taking the studied drink with antioxidant properties under incrementally increasing submaximal exercise test conditions contributed to the stabilization of the maximum and average velocity indicators in the breath-holding test, approaching to the background pre-exercise values of the minimum velocity indicator in the hyperventilation test, as well as to the “return” to the pre-exercise values of the pulsatility index in the torsion test from both sides.

The studied glucose-electrolyte composition has a homeostatic effect, probably due to the effect on the mechanisms of homeostatic regulation of vascular tone, affecting endothelial reactivity, pH level stabilization, oxidative phosphorylation.

Source of funding

The research was carried out with the financial support of the Ministry of Science and Higher Education of the Russian Federation, Priority-2030 program No. 075-15-2021-1323.

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

1. Jarvis SS, Levine BD, Prisk GK, Shykoff BE, Elliott AR, Rosow E, et al. Simultaneous determination of the accuracy and precision of closed-circuit output rebreathing techniques. *J Appl Physiol*. 2007; 103: 867-874. doi: 10.1152/japplphysiol.01106.2006

2. Smith KJ, Wildfong KW, Hoiland RL, Harper M, Lewis NC, Pool A, et al. Role of CO_2 in the cerebral hyperemic response to incremental normoxic and hyperoxic exercise. *J Appl Physiol.* 2016; 120: 843-854. doi: 10.1152/japplphysiol.00490.2015

3. Ito H, Yokoyama I, Iida H, Kinoshita T, Hatazawa J, Shimosegawa E, et al. Regional differences in cerebral vascular response to $PaCO_2$ changes in humans measured by positron emission tomography. *J Cereb Blood Flow Metab*. 2000; 20: 1264-1270. doi: 10.1097/00004647-200008000-00011

4. Hew-Butler T. Exercise-associated hyponatremia. *Front Horm Res*. 2019; 52: 178-189. doi: 10.1159/000493247

5. James LJ, Moss JH. Hypohydration impairs endurance performance: A blinded study. *Physiol Rep.* 2017; 5(12): e13315. doi: 10.14814/phy2.13315

6. Watso JC, Farquhar WB. Hydration status and cardiovascular function. *Nutrients.* 2019; 11(8): 1866. doi: 10.3390/nu11081866

7. Martinchik AN, Baeva VS, Peskova EV, Kudryavtseva KV, Denisova NN, Lavrinenko SV, et al. Actual liquid consumption by highly qualified athletes in the mode of the training process. *Problems of Nutrition.* 2018; 87(3): 36-44. (In Russ.). doi: 10.24411/0042-8833-2018-10029

8. Vykhodets IT, Kurashvili VA, Miroshnikova YuV. *Clinical recommendations on the methods of rehydration of the athlete's body in various Olympic sports during training events and sports competitions.* Moscow; 2018. (In Russ.).

9. *Report of Science Committee on Food on composition and specification of food in tended to meet the expenditure of intense muscular effort, especially for sportsmen.* 2001.

10. Maughan RJ, Murray R. *Sports drinks: Basic science and practical aspects*. Boca Raton: CRC Press; 2019.

11. Thein-Nissenbaum J, Hammer E. Treatment strategies for the female athlete triad in the adolescent athlete: Current perspectives. *Open Access J Sports Med.* 2017; 8: 85-95. doi: 10.2147/OAJSM.S100026

12. Sawka MN, Greenleaf JE. Current concepts concerning thirst, dehydration, and fluid replacement: Overview. *Med Sci Sports Exerc.* 1992; 24(6): 643-644.

13. Mason SA, Trewin AJ, Parker L, Wadley GD. Antioxidant supplements and endurance exercise: Current evidence and mechanistic insights. *Redox Biol*. 2020; 35: 101471. doi: 10.1016/j.redox.2020.101471

14. Sellami M, Slimeni O, Pokrywka A, Kuvačić G, Hayes LD, Milic M. Herbal medicine for sports: A review. *J Int Soc Sports Nutr*. 2018; 15(15): 14. doi: 10.1186/s12970-018-0218-y

15. Smith KJ, MacLeod D, Willie CK, Lewis NCS, Hoiland RL, Ikeda K, et al. Influence of high altitude on cerebral blood flow and fuel utilization during exercise and recovery. *J Physiol*. 2014; 592: 5507-5527. doi: 10.1113/jphysiol.2014.281212

16. Ogoh S, Dalsgaard MK, Yoshiga CC, Dawson EA, Keller DM, Raven PB, et al. Dynamic cerebral autoregulation during exhaustive exercise in humans. *Am J Physiol Heart Circ Physiol*. 2005; 288: 1461-1467. doi: 10.1152/ajpheart.00948.2004

17. Kim VN, Krivulina GB, Prosekin GA. The effect of dehydration on the development of endothelial dysfunction in young athletes: A comparative analysis of the effectiveness of a new honey isotonic drink and standard means of restoring hydro-electrolytic balance. *Acta biomedica scientifica*. 2020; 5(5): 86-98. (In Russ.). doi: 10.29413/abs.2020-5.5.12

18. Bachi AL, Sierra AP, Rios FJ, Gonçalves DA, Ghorayeb N, Abud RL. Athletes with higher VO_2max present reduced oxLDL after a marathon race. *BMJ Open Sport Exerc Med*. 2015; 1(1): bmjsem-2015-000014. doi: 10.1136/bmjsem-2015-000014

19. Green DJ, Hopman MT, Padilla J, Laughlin MH. Vascular adaptation to exercise in humans: Role of hemodynamic stimuli. *Physiol Rev*. 2017; 97(2): 495-528. doi: 10.1152/physrev.00014.2016

20. Lopatin ZV, Vasilenko VS. Endothelial dysfunction markers in an athlete in training load. *Modern Problems of Science and Education*. 2019; 1: 414-416. (In Russ.).

21. Smith AD, Refsum H. Homocysteine, B vitamins, and cognitive impairment. *Annu Rev Nutr*. 2016; 36: 211-239. doi: 10.1146/annurev-nutr-071715-050947

22. Laughlin MH, Newcomer SC, Bender SB. Importance of hemodynamic forces as signals for exercise-induced changes in endothelial cell phenotype. *J Appl Physiol*. 2008; 104(3): 588-600. doi: 10.1152/japplphysiol.01096.2007

23. Rezk-Hanna M, Seals DR, Rossman MJ, Gupta R, Nettle ChO, Means A. Ascorbic acid prevents vascular endothelial dysfunction induced by electronic hookah (waterpipe) vaping. *J Am Heart Assoc*. 2021; 10(5): e019271. doi: 10.1161/JAHA.120.019271

24. Naimi M, Vlavcheski F, Shamshoum H. Rosemary extract as a potential anti-hyperglycemic agent: Current evidence and future perspectives. *Nutrients*. 2017; 1(9): 968. doi: 10.3390/nu9090968

25. Prasannarong M, Saengsirisuwan V, Surapongchai J, Chukijrungroat BJ, Rattanavichit Y, et al. Rosmarinic acid improves hypertension and skeletal muscle glucose transport in angiotensin II-treated rats. BMC. *Complement Altern Med*. 2019; 19(1): 165. doi: 10.1186/s12906-019-2579-4

26. Seyydi SM, Tofighi A, Rahmati M. Exercise and Urtica Dioica extract ameliorate mitochondrial function and the expression of cardiac muscle nuclear respiratory factor 2 and peroxisome proliferator-activated receptor gamma coactivator 1-alpha in STZ-induced diabetic rats. *Gene*. 2022; 15(822): 146351. doi: 10.1016/j.gene.2022.146351

27. Liang Y, Qiu J, Gao HQ. Protective effect of grape seed proanthocyanidins extracts on reperfusion arrhythmia in rabbits. *J Nutr Sci Vitaminol (Tokyo)*. 2009; 55(3): 223-230. doi: 10.3177/jnsv.55.223

28. Quinones M. The polyphenols, naturally occurring compounds with beneficial effects on cardiovascular disease. *Nutr Hosp*. 2012; 27(1): 76-89. doi: 10.1590/S0212-16112012000100009

29. Kang P, Ryu K-H, Jeong-Min Lee, Kim HK, Seol GH, et al. Endothelium- and smooth muscle-dependent vasodilator effects of *Citrus aurantium* L. var. amara: Focus on Ca(2+) modulation. *Biomed Pharmacother*. 2016; 82: 467-71. doi: 10.1016/j.biopha.2016.05.030

30. Khoo NK. Dietary flavonoid quercetin stimulates vasorelaxation in aortic vessels. *Free Radic Biol Med*. 2010; 49(3): 339-347. doi: 10.1016/j.freeradbiomed.2010.04.022

ЛИТЕРАТУРА

1. Jarvis SS, Levine BD, Prisk GK, Shykoff BE, Elliott AR, Rosow E, et al. Simultaneous determination of the accuracy and precision of closed-circuit output rebreathing techniques. *J Appl Physiol*. 2007; 103: 867-874. doi: 10.1152/japplphysiol.01106.2006

2. Smith KJ, Wildfong KW, Hoiland RL, Harper M, Lewis NC, Pool A, et al. Role of CO_2 in the cerebral hyperemic response to incremental normoxic and hyperoxic exercise. *J Appl Physiol*. 2016; 120: 843-854. doi: 10.1152/japplphysiol.00490.2015

3. Ito H, Yokoyama I, Iida H, Kinoshita T, Hatazawa J, Shimosegawa E, et al. Regional differences in cerebral vascular response to $PaCO_2$ changes in humans measured by positron emission tomography. *J Cereb Blood Flow Metab*. 2000; 20: 1264-1270. doi: 10.1097/00004647-200008000-00011

4. Hew-Butler T. Exercise-associated hyponatremia. *Front Horm Res*. 2019; 52: 178-189. doi: 10.1159/000493247

5. James LJ, Moss JH. Hypohydration impairs endurance performance: A blinded study. *Physiol Rep*. 2017; 5(12): e13315. doi: 10.14814/phy2.13315

6. Watso JC, Farquhar WB. Hydration status and cardiovascular function. *Nutrients*. 2019; 11(8): 1866. doi: 10.3390/nu11081866

7. Мартинчик А.Н., Баева В.С., Пескова Е.В., Кудрявцева К.В., Денисова Н.Н., Лавриненко С.В., и др. Фактическое потребление жидкости спортсменами высокой квалификации в режиме тренировочного процесса. *Вопросы питания*. 2018; 87(3): 36-44. doi: 10.24411/0042-8833-2018-10029

8. Выходец И.Т., Курашвили В.А., Мирошникова Ю.В. *Клинические рекомендации по методикам регидрата-*

ции организма спортсмена в различных олимпийских видах спорта во время тренировочных мероприятий и спортивных соревнований. М.; 2018.

9. *Report of Science Committee on Food on composition and specification of food in tended to meet the expenditure of intense muscular effort, especially for sportsmen.* 2001.

10. Maughan RJ, Murray R. *Sports drinks: Basic science and practical aspects*. Boca Raton: CRC Press; 2019.

11. Thein-Nissenbaum J, Hammer E. Treatment strategies for the female athlete triad in the adolescent athlete: Current perspectives. *Open Access J Sports Med.* 2017; 8: 85-95. doi: 10.2147/OAJSM.S100026

12. Sawka MN, Greenleaf JE. Current concepts concerning thirst, dehydration, and fluid replacement: Overview. *Med Sci Sports Exerc.* 1992; 24(6): 643-644.

13. Mason SA, Trewin AJ, Parker L, Wadley GD. Antioxidant supplements and endurance exercise: Current evidence and mechanistic insights. *Redox Biol.* 2020; 35: 101471. doi: 10.1016/j.redox.2020.101471

14. Sellami M, Slimeni O, Pokrywka A, Kuvačić G, Hayes LD, Milic M. Herbal medicine for sports: A review. *J Int Soc Sports Nutr*. 2018; 15(15): 14. doi: 10.1186/s12970-018-0218-y

15. Smith KJ, MacLeod D, Willie CK, Lewis NCS, Hoiland RL, Ikeda K, et al. Influence of high altitude on cerebral blood flow and fuel utilization during exercise and recovery. *J Physiol.* 2014; 592: 5507-5527. doi: 10.1113/jphysiol.2014.281212

16. Ogoh S, Dalsgaard MK, Yoshiga CC, Dawson EA, Keller DM, Raven PB, et al. Dynamic cerebral autoregulation during exhaustive exercise in humans. *Am J Physiol Heart Circ Physiol.* 2005; 288: 1461-1467. doi: 10.1152/ajpheart.00948.2004

17. Ким В.Н., Кривулина Г.А., Просекин Г.Б. Влияние обезвоживания на развитие дисфункции эндотелия у юных спортсменов: сравнительный анализ эффективности нового медового изотонического напитка и общепринятых средств восстановления водно-электролитного баланса. *Acta biomedica scientifica.* 2020; 5(5): 86-98. doi: 10.29413/abs.2020-5.5.12

18. Bachi AL, Sierra AP, Rios FJ, Gonçalves DA, Ghorayeb N, Abud RL. Athletes with higher VO_2max present reduced oxLDL after a marathon race. *BMJ Open Sport Exerc Med.* 2015; 1(1): bmjsem-2015-000014. doi: 10.1136/bmjsem-2015-000014

19. Green DJ, Hopman MT, Padilla J, Laughlin MH. Vascular adaptation to exercise in humans: Role of hemodynamic stimuli. *Physiol Rev.* 2017; 97(2): 495-528. doi: 10.1152/physrev.00014.2016

20. Лопатин З.В., Василенко В.С. Маркеры эндотелиальной дисфункции у спортсменов при тренировочных нагрузках. *Современные проблемы науки и образования.* 2019; 1: 414-416.

21. Smith AD, Refsum H. Homocysteine, B vitamins, and cognitive impairment. *Annu Rev Nutr*. 2016; 36: 211-239. doi: 10.1146/annurev-nutr-071715-050947

22. Laughlin MH, Newcomer SC, Bender SB. Importance of hemodynamic forces as signals for exercise-induced changes in endothelial cell phenotype. *J Appl Physiol.* 2008; 104(3): 588-600. doi: 10.1152/japplphysiol.01096.2007

23. Rezk-Hanna M, Seals DR, Rossman MJ, Gupta R, Nettle ChO, Means A. Ascorbic acid prevents vascular endothelial dysfunction induced by electronic hookah (waterpipe) vaping. *J Am Heart Assoc.* 2021; 10(5): e019271. doi: 10.1161/JAHA.120.019271

24. Naimi M, Vlavcheski F, Shamshoum H. Rosemary extract as a potential anti-hyperglycemic agent: Current evidence and future perspectives. *Nutrients.* 2017; 1(9): 968. doi: 10.3390/nu9090968

25. Prasannarong M, Saengsirisuwan V, Surapongchai J, Chukijrungroat BJ, Rattanavichit Y, et al. Rosmarinic acid improves hypertension and skeletal muscle glucose transport in angiotensin II-treated rats. BMC. *Complement Altern Med.* 2019; 19(1): 165. doi: 10.1186/s12906-019-2579-4

26. Seyydi SM, Tofighi A, Rahmati M. Exercise and Urtica Dioica extract ameliorate mitochondrial function and the expression of cardiac muscle nuclear respiratory factor 2 and peroxisome proliferator-activated receptor gamma coactivator 1-alpha in STZ-induced diabetic rats. *Gene.* 2022; 15(822): 146351. doi: 10.1016/j.gene.2022.146351

27. Liang Y, Qiu J, Gao HQ. Protective effect of grape seed proanthocyanidins extracts on reperfusion arrhythmia in rabbits. *J Nutr Sci Vitaminol (Tokyo).* 2009; 55(3): 223-230. doi: 10.3177/jnsv.55.223

28. Quinones M. The polyphenols, naturally occurring compounds with beneficial effects on cardiovascular disease. *Nutr Hosp.* 2012; 27(1): 76-89. doi: 10.1590/S0212-16112012000100009

29. Kang P, Ryu K-H, Jeong-Min Lee, Kim HK, Seol GH, et al. Endothelium- and smooth muscle-dependent vasodilator effects of *Citrus aurantium* L. var. amara: Focus on Ca(2+) modulation. *Biomed Pharmacother.* 2016; 82: 467-71. doi: 10.1016/j.biopha.2016.05.030

30. Khoo NK. Dietary flavonoid quercetin stimulates vasorelaxation in aortic vessels. *Free Radic Biol Med.* 2010; 49(3): 339-347. doi: 10.1016/j.freeradbiomed.2010.04.022

Information about the authors

Natalia S. Tribrat – Cand. Sc. (Biol.), Associate Professor at the Department of the Human and Animal Physiology and Biophysics, V.I. Vernadsky Crimean Federal University, e-mail: miu-miu07@mail.ru, https://orcid.org/0000-0002-6800-1419

Elena A. Birukova – Cand. Sc. (Biol.), Associate Professor at the Department of the Human and Animal Physiology and Biophysics, V.I. Vernadsky Crimean Federal University, e-mail: biotema@mail.ru, https://orcid.org/0000-0002-2628-0923

Denis R. Khusainov – Cand. Sc. (Biol.), Associate Professor at the Department of the Human and Animal Physiology and Biophysics, V.I. Vernadsky Crimean Federal University, e-mail: gangliu@yandex.ru, https://orcid.org/0000-0003-0974-6792

Nikolay P. Mishin – Senior Lecturer at the Department of Theory and Methods of Physical Culture, V.I. Vernadsky Crimean Federal University, e-mail: mishinnick@yandex.ru, https://orcid.org/0000-0003-4033-1157

Elena I. Nagaeva – Cand. Sc. (Biol.), Associate Professor at the Department of Theory and Methods of Physical Culture, V.I. Vernadsky Crimean Federal University, e-mail: enagaeva75@mail.ru, https://orcid.org/0000-0003-0192-1752

Elena V. Burtseva – Associate Professor at the Department of Pharmacology, V.I. Vernadsky Crimean Federal University, e-mail: burtsevaev2009@yandex.ru, https://orcid.org/0000-0002-5418-7849

Semen K. Kushnir – Student, Kazan State Medical University, e-mail: pulpit@list.ru, https://orcid.org/0000-0002-3978-6093