DOI: 10.14739/mmt.2025.1.314534 Огляд літератури / Reviews of literature
UDC 612.766.1.015.3:547.472.3:796.8.071.2

The role of lactate in the body of martial artists during physical activity: a new look at the problem

I. F. Bielenichev[1,A,D,E], L. M. Gunina[2,C,F], O. I. Orlov[2,B], I. B. Samura*[1,D,F], E. Yu. Doroshenko[1,C], S. I. Danylchenko[3,D], D. Yu. Skoryna[1,B]

[1]Zaporizhzhia State Medical and Pharmaceutical University, Ukraine, [2]State Tax University, Irpin, Ukraine, [3]Kherson State University, Ukraine

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

Keywords:
martial artists, lactate, delayed onset muscle soreness (DOMS), oxidative stress, inflammation.

Ключові слова:
спортсмени-єдиноборці, лактат, відстрочена м'язова болючість (DOMS), оксидативний стрес, запалення.

Надійшла до редакції / Received: 06.11.2024

Після доопрацювання / Revised: 23.12.2024

Схвалено до друку / Accepted: 10.01.2025

Конфлікт інтересів:
відсутній.

Conflicts of interest:
authors have no conflict of interest to declare.

***E-mail:**
irinasamura77@gmail.com

Aim. To conduct a modern semantic analysis of the results of our own research and literature data on the physiological significance of increased lactate level in skeletal muscles during physical activity in martial artists.

Materials and methods. This study used bibliosemantic, analytical, logical, and generalization methods. The bibliographic databases of life sciences and biomedical information MEDLINE, EMBASE, Medline (PubMed), Web of Science, and Cochrane Central were searched to find publications in English that matched the research keywords. The authors carried out an independent search and selection of articles, assessment of data quality, compliance of the presentation and interpretation with the main idea of the study, with the formation of the final list of references.

Results. For many years, the role of lactate in the formation of physical fatigue and delayed muscle soreness in martial artists and other athletes remained unknown. There has been a lot of speculation and competing concepts. Over the past 20 years, due to the successes of modern biochemistry, physiology, and molecular pharmacology, subtle molecular-biochemical mechanisms of delayed muscle soreness formation after muscle loading have been revealed. However, a holistic attitude to the role of lactate has not been formulated. We analyzed the results of modern studies, which showed that oxidative stress, inflammation, and a decrease in cytoprotective proteins, in particular HSP_{70}, but not the accumulation of lactate, are more important in the formation of delayed onset muscle soreness (DOMS).

Conclusions. Accumulation of lactate in muscle cells with its subsequent release into the bloodstream is considered to be much more positive than negative factor, and therefore the views on the increase of lactate content and its assessment as an enemy of athletes, including martial artists, should be reconsidered.

Modern medical technology. 2025;17(1):51-59

Роль лактату в організмі майстрів єдиноборств під час фізичних навантажень: новий погляд на проблему

І. Ф. Бєленічев, Л. М. Гуніна, О. І. Орлов, І. Б. Самура, Е. Ю. Дорошенко, С. І. Данильченко, Д. Ю. Скорина

Мета роботи – здійснити сучасний семантичний аналіз результатів власних досліджень і відомостей фахової літератури щодо фізіологічного значення підвищеного рівня лактату в м'язах під час фізичних навантажень у єдиноборців.

Матеріали і методи. Під час роботи використано бібліосемантичний, аналітичний, логічний методи, а також узагальнення. Здійснили пошук публікацій англійською мовою, що відповідають ключовим словам дослідження, у бібліографічних базах даних наук про життя та біомедичної інформації MEDLINE, EMBASE, Medline (PubMed), Web of Science і Cochrane Central. Автори здійснили самостійний пошук і відбір статей, оцінювання якості даних, відповідності викладу й інтерпретації основній ідеї дослідження з формуванням остаточного списку літератури.

Результати. Багато років роль лактату у формуванні фізичної втоми та відстроченої м'язової болючості у єдиноборців і представників інших видів спорту залишалася невідомою. У науковій літературі було багато спекуляцій і концепцій, що конкурували. Протягом останніх 20 років завдяки науковим досягненням у галузі біохімії, фізіології, молекулярної фармакології дедалі більше розкривають тонкі молекулярно-біохімічні механізми формування відстроченої м'язової болючості (DOMS) після м'язових навантажень. Втім цілісної одностайної концепції щодо ролі лактату досі не сформульовано. Проаналізували результати сучасних досліджень, де показано, що у формуванні відстроченої болючості м'язів більше значення мають оксидативний стрес, запалення, зниження рівнів цитопротективних білків, зокрема HSP_{70}, а не накопичення лактату.

Висновки. Накопичення лактату у м'язових клітинах із наступним викидом його в кровообіг є значно більш позитивним, ніж негативним чинником, і тому застрілі погляди на зростання вмісту лактату та визначення його як ворога спортсменів, зокрема спортсменів-єдиноборців, доцільно переглянути.

Сучасні медичні технології. 2025. Т. 17, № 1(64). С. 51-59

For more than 120 years, the diverse role of lactate in the formation of physical fatigue and delayed onset muscle soreness (DOMS) has been mysterious and raises many questions and speculations among physiologists, pathophysiologists, pharmacologists and specialists in the field of physical education. It is axiomatic among the sports and medical community that an increase in lactate in muscles after training or physical activity is the main cause of muscle fatigue and soreness. Medical and non-medical approaches have been developed to utilize lactate from muscles. Over the past 20 years, scientific works have appeared that reveal the subtle molecular biochemical mechanisms of DOMS formation after muscle contractions [1].

Data have emerged that "rehabilitate" lactate and shed light on its role in DOMS. DOMS is defined as a delayed onset of soreness, muscle stiffness, swelling, loss of ability to generate force, decreased range of joint movements, and decreased proprioceptive function in martial artists. DOMS pain occurs within 8 hours after unaccustomed or strenuous exercise, peaks after 1 or 2 days, and subsides within a week [2]. Several competing hypotheses have been proposed about the reasons and mechanisms responsible for DOMS, including the involvement of lactate in this process. However, a comprehensive understanding of the role of lactate has not been formulated.

Aim

To conduct a modern semantic analysis of the results of our own research and literature data on the physiological significance of increased lactate level in skeletal muscles during physical activity in martial artists.

Materials and methods

This study used bibliosemantic, logical, analytical, and generalization methods. The bibliographic databases of life sciences and biomedical information MEDLINE, EMBASE, Medline (PubMed), Web of Science, and Cochrane Central were searched to find publications in English that matched the research keywords. The authors carried out an independent search and selection of articles, assessment of data quality, compliance of the presentation and interpretation with the main idea of the study, with the formation of the final list of references.

Results

Our body always, and especially during physical loading, needs energy for the functioning of all organs and the contraction of skeletal muscles. Carbohydrates, the main energy substrates, enter the body with food, and are broken down in the intestine to glucose, which then enters the blood and is transported to all types of cells in the body, including skeletal muscle cells [3]. In the cytoplasm of cell, glycolysis occurs – the oxidation of glucose to pyruvate (pyruvic acid, PA) with the formation of ATP [4]. Then, due to the lactate dehydrogenase (LDH) enzyme, pyruvate is reduced to lactic acid, which immediately loses a hydrogen ion and can add sodium (Na^+) or potassium (K^+) ions, and turn into a salt of lactic acid – lactate *(Fig. 1)*.

As can be seen in *Fig. 1*, lactic acid and lactate are not identical substances. It is lactate that accumulates in the muscles, is eliminated from them and transformed, so it is incorrect to talk about lactic acid in the muscles [5,6]. Until 1970, lactate was considered a byproduct formed in working muscles due to a lack of oxygen. However, research over the last decades has disproved this claim. For example, in 2015, Matthew J. Rogatzky et al. found that glycolysis always ends with the formation of lactate [7,8]. Thus, scientists working under his leadership postulate that "...through much of the history of metabolism, lactate [La(–)] has been considered merely a dead-end waste product during periods of dysoxia. Congruently, the end product of glycolysis has been viewed dichotomously: pyruvate in the presence of adequate oxygenation, La(–) in the absence of adequate oxygenation. In contrast, given the near-equilibrium nature of the LDH reaction and that LDH has a much higher activity than the putative regulatory enzymes of the glycolytic and oxidative pathways, we contend that La(-) is always the end product of glycolysis". This is also stated by the outstanding American sports biochemist George A. Brooks from the University of California, who has been studying lactate for more than 30 years [9,10,11].

Lactate and glucose can be interconverted in the processes of glycolysis and gluconeogenesis. One logical way to coordinate these processes is as follows: most cells extract energy from carbohydrates by taking up glucose and completely oxidizing it to carbon dioxide (CO_2). Cells facing particularly acute energy demands take up additional glucose and release some lactate as a waste product. In addition, as Gertie and Corey showed, hungry muscles release glycogen stores as lactate; then the liver "cleans" this lactate, converting it back into glucose. In this scenario, lactate has value only as a substrate for glucose formation. The above strategy provides clear expectations for metabolic flow in mammals: tissue glucose uptake should significantly exceed lactate uptake, and the rate of the whole-body lactate production should be approximately equal liver and kidney utilization of lactate to maintain gluconeogenesis [12].

Lactate accumulation in the muscle, then sequentially in blood, reflects only the balance between its synthesis and excretion, and is not related to aerobic or anaerobic mechanisms of energy production. Lactate is always produced during glycolysis regardless of the presence or absence (deficiency) of oxygen: it is produced even when the muscle is at rest [13].

Does lactate increase muscle pain? Although from a scientific point of view, this narrative has been denied for a long time, there are widespread claims at the household level that lactate is to blame for the onset of muscle pain after exercise or, more precisely, according to the modern consolidated scientific judgments, syndromes of exercise-induced muscle damage (EIMD) and DOMS. These are two well-known syndromes in sports today, capable, regardless of the sports type and individual characteristics of the athlete, to accelerate the onset of fatigue and the corresponding decrease in physical performance in martial artists and other athletes [14].

EIMD and DOMS are closely related as cause and effect [15]. Isometric and concentric exercises contribute to the development of EIMD, but eccentric loads are most important for the development of muscle damage. There is a point of view that

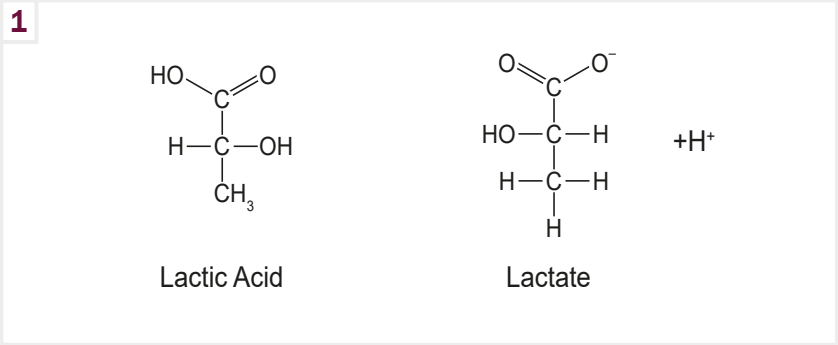

Fig. 1. The structure of lactic acid and its salt – lactate.

such violations of myocytes structure and function, associated with inflammation and increased protein metabolism, are short-term (a few days), and can contribute to muscle adaptation and hypertrophy [16].

The first mention of DOMS was made by the American physician Theodore Hough in 1902. He stated that when "untrained skeletal muscles are exercised, this often leads to discomfort that does not become apparent until 8–10 hours after exercise", and concluded that this could not be due to fatigue alone. Since Theodore Hough's initial observation, there has been an increase in research on DOMS, and yet its exact etiology remains unclear. The first weighted judgments regarding the mechanisms of DOMS development were proposed in 1984 as follows:

1. intense muscle loads (especially associated with eccentric exercises) in the contractile / elastic system of muscles lead to structural damage;

2. damage to the cell membrane of myocytes is accompanied by an imbalance of homeostasis of calcium ions (Ca^{2+}) in damaged muscle fibers, which leads to necrosis, the severity of which reaches its peak about 2 days after training;

3. products of macrophage activity and intracellular contents of myocytes accumulate in the interstitium due to increased permeability of the cell membrane, and this, in turn, stimulates free nerve endings of group IV sensory neurons in the muscles, leading to the sensation of pain in DOMS [17], which later turned out to be not far from the truth.

DOMS has long been considered as not only an adaptive response to physical loading, especially in the retracting and retracting-developing mesocycles of the preparatory period, but also as an inevitable element of intense loads during professional and amateur training. On the contrary, the appearance of these syndromes, as evidenced by the data of a systematic review of the literature, in many situations slows recovery after training, reduces further growth of physical fitness [14]. These circumstances are especially important under the set conditions of training loads intensification, even with their timeliness, in the dynamics of the annual macrocycle and long-term improvement of modern sports both in general and in the particular training process of each individual qualified athlete.

Currently there is no doubt that vigorous or prolonged physical loading, especially with elements of eccentric movements, with a mismatch between the level of load and the degree of muscle adaptation, is accompanied by varying degree of microdamage of myofibrils and DOMS. Syndrome of DOMS, also known as "muscle fever" is characterized by soreness in the muscles, especially after previously non-performed and/or unusual high-intensity exercises [18]. DOMS syndrome typically develops after the end of physical activity; and it peaks between 24 and 48 hours after a training session or competition. Symptoms of DOMS include decreased muscle strength, pain, muscle weakness, decreased mobility, and swelling in the painful area, as well as the formation of a biochemical response in the form of an increased activity of the specific muscle enzymes creatine kinase and lactate dehydrogenase, as well as aspartate and alanine aminotransferase [19].

The results of recent studies confirm that in high-level sports, ultrastructural muscle injuries, including manifestations of the DOMS syndrome, are the cause of a decrease in the contractile ability of skeletal muscles, and, therefore, in the performance of athletes including combat martial artists [20]. Moreover, the role of DOMS in the occurrence of injuries is also quite significant: reduced range of motion caused by the presence of pain, characteristic of DOMS syndrome, can lead to the inability to effectively perceive stimuli that affect the physical activity and injury of the athlete. Changes in mechanical movement can increase the load on soft tissue structures, and a decrease in the initial level of muscle power may signal a compensatory, unregulated increase in the diameter of muscle fibers beyond the limits of working muscle hypertrophy, which leads to an unusual load on the muscle with subsequent injury [21].

The etiology of DOMS has not been fully elucidated, although it is known that the trigger mechanisms of this process are biochemical intracellular changes and inflammation due to the formation of EIMD. For many years, DOMS was mistakenly thought to simply be the result of lactate accumulation in muscle tissue (what athletes call "krepatura") during intense exercise. Acid-sensing ion channels (ASICs) play an important role in the physiology and biochemistry of muscle fatigue. ASICs in afferent muscles are activated by H^+ and other chemicals and play a role in the development of immediate exercise-induced pain (IEIP) but not DOMS [22]. ASICs expressed during ischemia or exercise are formed as homotrimers or heterotrimers and have several isoforms (ASIC1a, ASIC1b, ASIC2a, ASIC2b, and ASIC3), where each channel displays different properties. These channels play a protective role in preventing muscle damage associated with

intense exercise [23]. ASICs are tuned to sense chemical changes in skeletal muscle; they are activated in the extracellular pH range between 7.0 and 6.8, which occurs during muscle ischemia or exercise, and are enhanced by other chemicals (lactate, ATP, arachidonic acid, and NO) during muscle ischemia, hypoxia or exercise [22].

Current ideas about the nature of DOMS differ significantly from the original. Pain, mobility limitation, difficulty in performing repeated exercise cycles due to DOMS, on the one hand, and lactate accumulation, on the other hand, were found to be completely unrelated [24]. The concentration of lactate in the blood and muscles after intense concentric anaerobic and, especially, eccentric loads does increase, but it returns to normal, i. e. the initial values of a particular athlete, which were before the load, quite quickly – within 1.0–1.5 hours. At the same time, the severity of DOMS manifestations increases during the first 24 hours, reaching a peak between 24 and 48 hours, when blood serum lactate levels are already within the normal range for athletes [25,26]. In our opinion, it can be assumed that the accumulation of lactate in blood serum with a decrease in the pH of the medium, i. e. plasma and interstitial fluid in combat athletes, only triggers a whole cascade of various biochemical reactions, which subsequently form the symptom complex characteristic of DOMS. At the same time, we believe that various trigger mechanisms provoking further inflammation and the formation of this syndrome may be involved in connection with a highly individualized training program of adaptation of qualified martial artists to physical loads. Such a postulate to some extent can explain why DOMS does not occur in all athletes after the same direction and intensity of the load.

Oxidative stress plays an important role in the formation of DOMS. Thus, during intense physical exertion, the formation of reactive oxygen species (ROS) by mitochondria increases. Mitochondria, necessary for the production of ATP, become significant sources of ROS due to the leakage of electrons from their electron transport chain during increased activity, which potentially causes oxidative damage to protein molecules of receptors, ion channels, including ASIC. However, exercise also triggers protective mechanisms such as the superassembly of mitochondrial complex I in rats, which has been shown to reduce lipid peroxidation and oxidative damage to mitochondria, representing potential therapeutic benefits in metabolic diseases [27].

The role of the nitroxidergic system is also important. Moderate increases in NO synthesis enhance blood flow, oxygen delivery, and nutrient supply to muscles during exercise, enhancing performance and endurance. Regular aerobic exercise combined with nutritional supplements such as L-arginine and L-citrulline can counteract DOMS. Exercise-induced NO release also benefits vascular function and cardiovascular health, including patients with vascular diseases. Furthermore, NO promotes mitochondrial biogenesis and efficiency, which is critical for enhancing endurance and reducing fatigue during prolonged exercise [28,29,30].

The imbalance of iNOS/eNOS in DOMS leads to the formation of nitrosative stress, disruption of Ca^{2+} homeostasis in skeletal muscles, and S-nitrosylation of functional muscle proteins [31].

The data on the role of oxidative stress in DOMS settings were also confirmed by members of the scientific group under the leadership of Professor R. Deminice at the State University of Londrina (Brazil), known for his research in the field of free-radical oxidation during exercise in the study conducted in a randomized, double-blind, placebo-controlled (RDBPC) design with a high level of evidence, with course use of natural antioxidants [32]. The authors concluded that in this case antioxidants reduce the manifestation of oxidative stress and homeostasis disturbances mediated by it, which then lead to the deterioration of energy production processes, changes in the permeability of cell membranes, a decrease in the speed of nerve impulse conduction and, therefore, a slowing down of intermuscular and nerve-muscle interaction, etc.

It was also found that high-intensity and eccentric exercises significantly reduce the antioxidant protection of skeletal muscles and cause muscle damage, which leads to DOMS [33]. In particular, fluctuations in the activity of the antioxidant system in the enzymatic (glutathione peroxidase, glutathione reductase, superoxide dismutase) and non-enzymatic (reduced glutathione, ceruloplasmin) links, as well as excessive (in some athletes! – *author's note*) increase in cortisol content, and even insufficient intake of proteins, carbohydrates, unsaturated fats, vitamins, minerals, i.e. the main macro- and micronutrients, which are generally important for stimulating work capacity, may be of greater importance [34]. However, taking antioxidant supplements (vitamins E and C) does not reduce muscle soreness on the first day or one, two, three or four days after training [35].

Another study showed that the use of selenium, zinc, resveratrol, glutathione and N-acetylcysteine and their combinations in long courses of up to 6 weeks improves performance in high-level sports [33,36,37,38].

The antioxidant thiotriazoline, which reduces the formation of reactive oxygen species, increases the activity of superoxide dismutase and glutathione peroxidase, and protects muscle proteins from oxidative modification during working hypoxia, is of interest. Thiotriazoline activates the conversion of lactate to pyruvate, and is used before and during physical exercise to accelerate the removal of lactate from skeletal muscles and blood [39].

One of the common definitions of DOMS, formulated as "a consequence of mechanical and metabolic stress caused by physical activity" [40,41], gives practically nothing to understand the essence of this physiological (or pathophysiological? – *author's note*) process. Moreover, there is still no consensus on the relationship between muscle microdamage and DOMS, and there are both "pro" and "contra" arguments. The elimination of these phenomena, depending on the nature, intensity and duration of the previous load, can last from 3–4 to 7 days. Nevertheless, studies continue to consider DOMS as a direct or indirect result of muscle microdamage and EIMD formation.

Currently, one of the most popular schemes of the pathophysiological mechanism of DOMS development in eccentric type of muscle contraction was given in the recent problematic work of the head of the Department of Physical Culture and Sports Science at the University of Mohaghegh Ardebili (Iran), Professor A. Meamarbashi [42], which was also confirmed in later studies [43]. Microdamages of skeletal muscles in advanced EIMD syndrome

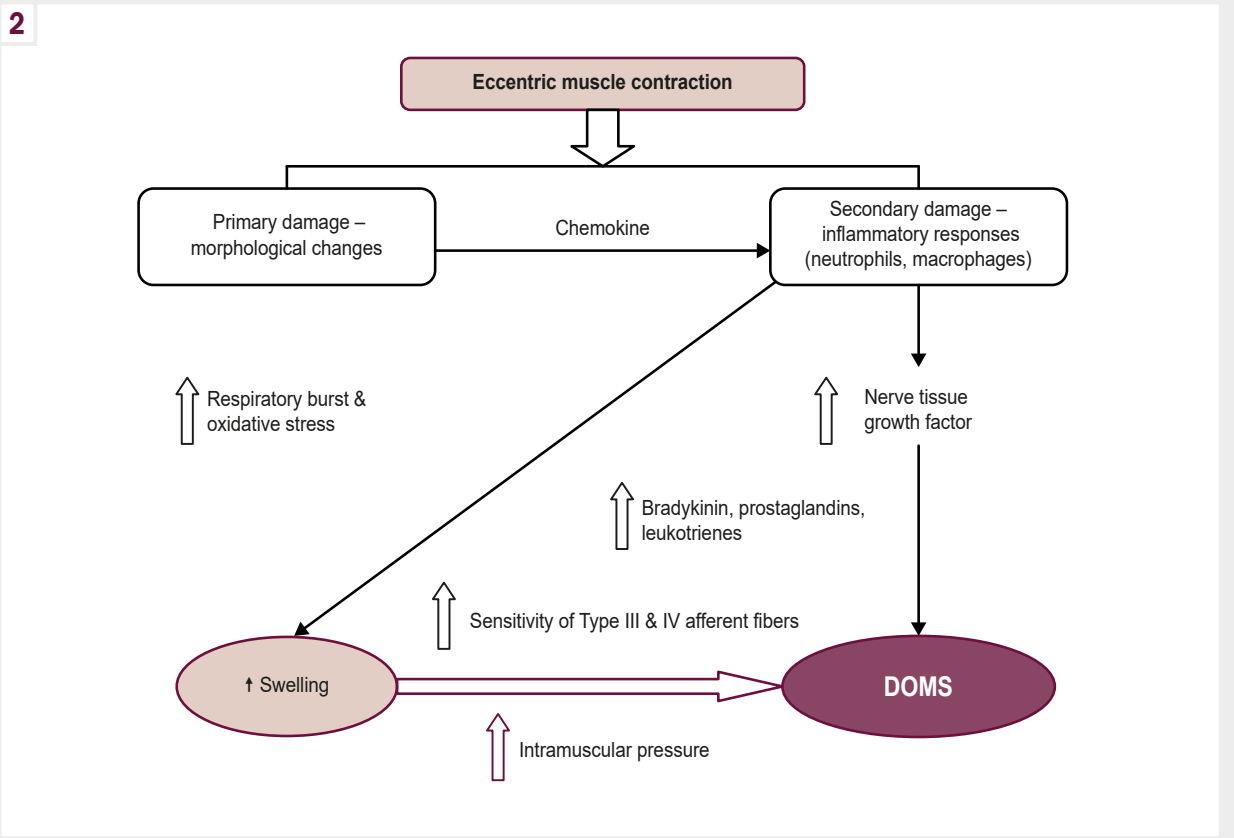

Fig. 2. General pathobiochemical and pathophysiological mechanisms of DOMS development (by Meamarbashi, 2017 [42]; modified by the authors).

trigger a cascade of biochemical reactions in the cells, in which an important role is played by an increase in the permeability of blood vessels (induced by release of bradykinin), activation of cyclooxygenase-2 (COX-2) and lipoxygenase with the formation of thromboxanes, prostaglandins and leukotrienes, as well as sensitization of nerve fibers of types III and IV with increased sensitivity to chemical and mechanical stimuli [44]. Edema, which also contributes to pain, as shown in *Fig. 2*, develops as a result of leakage of fluid from the lumen of vessels into tissues and accumulation of immune cells.

Violations in the structure of intracellular formations (sarcoplasmic reticulum, sarcomeres, myofibrils, etc.) are noted. Primary mechanical damage forms a pattern of secondary inflammatory response, in which bradykinin and nerve growth factors play a key role. From a clinical point of view, this process is a classic aseptic inflammation due to the action of physical (primarily, mechanical) factors.

From a biochemical point of view, the accumulation of neutrophils and macrophages in places of muscle fibers injury and their increased activity contributes to the rise of inflammatory mediators' content (bradykinins, prostaglandins, and leukotrienes). In particular, bradykinin activates phospholipase A2, and the concentration of Ca^{2+} ions in the cell membrane increases due to the opening of ion channels leading to the secretion of substance P [45]. In turn, substance P, one of the most well-known and researched peptides that have a number of functions, including pain perception, stimulates the production of arachidonic acid.

The relationship between DOMS, muscle damage, and inflammatory responses to eccentric exercise has been determined. Positive correlations were found between physical exercise and an increase in neutrophil migratory activity after 4 hours, and an increase in myoglobin and pro-inflammatory cytokines levels after 48 hours, which may be associated with muscle damage and inflammatory processes [40]. Further development of DOMS involved evaluation of the bradykinin B2 – nerve growth factor (NGF), and pathways of the neurotrophic factor derived from glial cell line-derived neurotrophic factor-2 (GDNF) pathways. Interaction between these routes occurred on two levels. The repeated pain attack effect was observed with strengthening the muscular mechanical withdrawal threshold (MMWT) and NGF, and this study suggested that adaptation might have occurred before the onset of bradykinin B2 receptor activation.

At the same time, the MMWT in the experiment decreased 1–3 days after lengthening muscle contractions. The results of changes in speed and range of stretch showed that muscle damage was rare, only under extreme conditions, and pure DOMS was formed with biochemical markers but without significant muscle damage when using antioxidants [46].

This leads to increased concentrations of prostaglandins and leukotrienes (pro-inflammatory effect of arachidonic acid). The

latter directly increase the sensitivity of afferent nerve fibers type III (muscle sensors of deep pressure according to the Lloyd-Hunt classification) and type IV (thin unmyelinated pain fibers).

In addition, leukotrienes increase the permeability of the vascular wall, which is accompanied by the adhesion of neutrophils to endothelial cells in the sites of injury. This enhances changes in cell membranes, increases intra-cellular pressure and causes the formation of edema with further secondary activation of type III and IV afferent fibers ultimately increasing the severity of the pain syndrome [42].

At first glance, it seems logical that some authors assumed that oxidative stress plays an important role in the pathogenesis of DOMS, but they were not confirmed by the results of the recent studies, although many studies indicate the presence of disorders of prooxidant-antioxidant balance in the syndromes of muscle microdamage and delayed muscle soreness [47,48]. Therefore, we believe that, at the moment, such studies are important to determine the significance of biomarkers in the diagnostic algorithm of DOMS.

To determine the severity of DOMS syndrome, the authors of the study examined a wide range of biochemical and hormonal indicators, such as creatine kinase, interleukin IL-6, tumor necrosis factor TNF-α, malondialdehyde (MDA); and serum iron, cortisol, testosterone, generally traditional for sports laboratory diagnosis [49,50]. The role of heat shock protein 70 (HSP_{70}) in the formation of DOMS is being studied. HSP_{70} is involved in the protection of macromolecules and their "correction" after oxidative modification, in the regulation and "prolongation" of compensatory shunts during working hypoxia [51]. There is also evidence that HSP_{70} released during exercise-induced DOMS activates the microglial TLR4 / IL-6 / TNF-α pathway in the spinal cord. Thus, blockade of TLR4 activation may be a novel strategy to prevent the development of DOMS before intense exercise [52]. HSP_{70} may serve as a biomarker to determine optimal exercise intensity in individuals with obesity or diabetes. HSP_{70} may have both pro- and anti-inflammatory effects during exercise and may increase or decrease DOMS [53].

Since modern researchers have been formed a consolidated point of view regarding the accumulation of lactate as a trigger mechanism for further successive homeostatic adjustments after physical load [54,55], in our opinion, it is inappropriate to exclude this indicator from the EIMD and DOMS diagnostic algorithm. There are recommendations to include the muscle form of creatine phosphokinase and myoglobin in laboratory monitoring of DOMS. A correlation was found between DOMS 24–96 hours after exercises for strength, flexion, and extension and myoglobin, and creatine phosphokinase activity [56]. For laboratory monitoring of DOMS, correlation analysis confirmed the prospects for determining markers of oxidative stress including MDA, carbonylated proteins, and oxidized glutathione [57].

The testing procedure is mandatory, including the determination of lactate content in the blood serum at rest, the level of vitamin D3 in the form of 25(OH)D3, and ionized calcium. In-depth and dynamic laboratory monitoring should play a primary role in the process of testing the presence and severity of EIMD and DOMS syndromes, as in this case blood serum indicators, namely, the content of the stress hormone cortisol, the main anabolic hormone testosterone; markers of inflammation, such as TNF-α, C-reactive protein; activity of enzymatic antioxidants and endogenous antioxidants; pro-inflammatory interleukins, bradykinin and prostaglandin F; activity of marker enzymes aspartate and alanine aminotransferases, gamma-glutamyl transpeptidase, lactate dehydrogenase, creatine phosphokinase, etc., significantly correlate with the severity of clinical manifestations of myofibril microdamage.

Understanding how a particular athlete responds to certain types of loads, as well as their volume and intensity, the coach can consciously manage the training process, and sports doctor and sports nutritionist can build an individual program of prevention and correction of fatigue, which will be the key to further growth of general and special performance and, accordingly, the competitive result of the athlete.

In fact, lactate levels drop significantly within minutes after the end of an exercise and return to normal completely some time afterward. Thus, lactate cannot cause muscle pain 24–72 hours after exercise. There is also a myth that lactate "acidifies" muscles and causes muscle fatigue. It is widely believed that the level of lactate in the blood affects the muscle performance. However, this is not actually from lactate, but from hydrogen ions that increase tissue acidity [58,59,60].

When the normal pH balance shifts to the acidic side, acidosis occurs. Many studies prove that acidosis negatively affects muscle contraction. In the "Biochemistry of exercise-induced metabolic acidosis", Robert A. Robergs et al. note that hydrogen ions are released whenever ATP is broken down to ADP and inorganic phosphate with the release of energy. When an athlete works at moderate intensity, hydrogen ions are used by muscle cell mitochondria for oxidative phosphorylation (reduction of ATP from ADP). When the intensity of exercises and the body's requirement for energy resources increase, ATP recovery occurs mainly due to the glycolytic and phosphagen systems. This causes an increased release of protons and, as a result, acidosis [61].

That is, the cause of the decrease in pH is not lactate, but a completely different mechanism. At the same time, researchers suggested that lactate helps to cope with acidosis because it can transport hydrogen ions from the cell. Thus, without increased lactate production, acidosis and muscle fatigue would occur much faster. Physical loading accompanied by fatigue causes acidosis, the accumulation of hydrogen ions, and the shift of the body's pH to the acidic side. Lactate, on the contrary, according to the most current views, helps overcome acidosis [62] and delay the onset of fatigue.

At the same time, lactate, contrary to unfounded fears about its negative impact on strength and power, creates favorable conditions for increasing muscle strength. The results of the study proved that a combined supplement of caffeine and lactate increases muscle growth even during low-intensity training by activating stem cells and anabolic signals: increasing the expression of myogenin and follistatin.

Conclusions

1. Thus, today the accumulation of lactate in muscle cells with its subsequent release into the bloodstream is considered to be

much more positive than negative factor, and therefore the views on the increase of lactate content and its assessment as an enemy of athletes, including martial artists, should be reconsidered.

2. We have also shown some molecular mechanisms of EIMD and DOMS formation, such as the involvement of heat shock proteins, reactive oxygen and nitrogen species, and products of oxidative modification of proteins. We have outlined the most rational ways of EIMD and DOMS pharmacocorrection.

Prospects for further research. The results obtained indicate the need for further research to clarify the role of lactate in the body of martial artists during physical activity that will serve as a theoretical basis for the development of new ways of pharmacocorrection of DOMS.

Funding

This study was funded by the Ministry of Health of Ukraine from the state budget.

Information about the authors:

Bielenichev I. F., PhD, DSc, Professor, Head of the Department of Pharmacology and Medical Formulation with Course of Normal Physiology, Zaporizhzhia State Medical and Pharmaceutical University, Ukraine.
ORCID ID: 0000-0003-1273-5314
Gunina L. M., PhD, DSc, Professor of the Department of Health Rehabilitation Technologies and Physical Education-Sports Rehabilitation, senior researcher; Head of the Educational Laboratory of Physical Rehabilitation and Ergotherapy, State Tax University, Irpin, Ukraine.
ORCID ID: 0000-0002-6207-1117
Orlov O. I., PhD, Associate Professor of the Department of Health Rehabilitation Technologies and Physical Education – Sports Rehabilitation, State Tax University, Irpin, Ukraine.
ORCID ID: 0009-0003-3965-2620
Samura I. B., MD, PhD, Associate Professor of the Department of Pharmacology and Medical Formulation with Course of Normal Physiology, Zaporizhzhia State Medical and Pharmaceutical University, Ukraine.
ORCID ID: 0000-0001-5352-3209
Doroshenko E. Yu., PhD, DSc, Professor, Head of the Department of Physical Rehabilitation, Sports Medicine, Physical Education and Health, Zaporizhzhia State Medical and Pharmaceutical University, Ukraine.
ORCID ID: 0000-0001-7624-531X
Danylchenko S. I., MD, PhD, Associate Professor of the Department of Medicine and Physical Therapy, Kherson State University, Ukraine.
ORCID ID: 0000-0001-5312-0231
Skoryna D. Yu., PhD, Associate Professor of the Department of Pharmaceutical, Organic and Bioorganic Chemistry, Zaporizhzhia State Medical and Pharmaceutical University, Ukraine.
ORCID ID: 0000-0002-8851-8757

Відомості про авторів:

Бєленічев І. Ф., д-р біол. наук, професор, зав. каф. фармакології та медичної рецептури з курсом нормальної фізіології, Запорізький державний медико-фармацевтичний університет, Україна.
Гуніна Л. М., д-р біол. наук, професор каф. технологій оздоровлення та фізкультурно-спортивної реабілітації, старший науковий співробітник; завідувач навчальної лабораторії фізичної реабілітації та ерготерапії, Державний податковий університет, м. Ірпінь, Україна.
Орлов О. І., канд. пед. наук, доцент каф. технологій оздоровлення та фізкультурно-спортивної реабілітації, Державний податковий університет, м. Ірпінь, Україна; заслужений тренер України.
Самура І. Б., канд. мед. наук, доцент каф. фармакології та медичної рецептури з курсом нормальної фізіології, Запорізький державний медико-фармацевтичний університет, Україна.
Дорошенко Е. Ю., д-р наук з фіз. виховання та спорту, професор, зав. каф. фізичної реабілітації, спортивної медицини, фізичного виховання та здоров'я, Запорізький державний медико-фармацевтичний університет, Україна.
Данильченко С. І., канд. мед. наук, доцент каф. фізичної терапії та ерготерапії, Херсонський державний університет, Україна.
Скорина Д. Ю., канд. фарм. наук, доцент каф. фармацевтичної, органічної та біоорганічної хімії, Запорізький державний медико-фармацевтичний університет, Україна.

References

1. Sonkodi B, Berkes I, Koltai E. Have we looked in the wrong direction for more than 100 years? Delayed onset muscle soreness is, in fact, neural microdamage rather than muscle damage. Antioxidants (Basel). 2020;9(3):212. doi: 10.3390/antiox9030212
2. Sonkodi B. Should we void lactate in the pathophysiology of delayed onset muscle soreness? Not so fast! Let's see a neurocentric view! Metabolites. 2022;9(12):857. doi: 10.3390/metabo12090857
3. Drozdowski LA, Thomson AB. Intestinal sugar transport. World J Gastroenterol. 2006;11(12):1657-70. doi: 10.3748/wjg.v12.i11.1657
4. Khattri RB, Puglise J, Ryan TE, Walter GA, Merritt ME, Barton ER. Isolated murine skeletal muscles utilize pyruvate over glucose for oxidation. Metabolomics. 2022;18(12):105. doi: 10.1007/s11306-022-01948-x
5. Levy B, Perez P, Gibot S, Gerard A. Increased muscle-to-serum lactate gradient predicts progression towards septic shock in septic patients. Intensive Care Med. 2010;36(10):1703-9. doi: 10.1007/s00134-010-1938-x
6. Cieminski K, Flis DJ, Dzik KP, Kaczor JJ, Wieckowski MR, Antosiewicz J, et al. Swim training affects on muscle lactate metabolism, nicotinamide adenine dinucleotides concentration, and the activity of NADH shuttle enzymes in a mouse model of amyotrophic lateral sclerosis. Int J Mol Sci. 2022;23(19):11504. doi: 10.3390/ijms231911504
7. Rogatzki MJ, Ferguson BS, Goodwin ML, Gladden LB. Lactate is always the end product of glycolysis. Front Neurosci. 2015;9:22. doi: 10.3389/fnins.2015.00022
8. Ferguson BS, Rogatzki MJ, Goodwin ML, Kane DA, Rightmire Z, Gladden LB. Lactate metabolism: historical context, prior misinterpretations, and current understanding. Eur J Appl Physiol. 2018;118(4):691-728. doi: 10.1007/s00421-017-3795-6
9. Brooks GA. The science and translation of lactate shuttle theory. Cell Metab. 2018;27(4):757-85. doi: 10.1016/j.cmet.2018.03.008
10. Brooks GA, Curl CC, Leija RG, Osmond AD, Duong JJ, Arevalo JA. Tracing the lactate shuttle to the mitochondrial reticulum. Exp Mol Med. 2022;54(9):1332-47. doi: 10.1038/s12276-022-00802-3
11. Chow LS, Gerszten RE, Taylor JM, Pedersen BK, van Praag H, Trappe S, et al. Reply to 'Lactate as a major myokine and exerkine'. Nat Rev Endocrinol. 2022;18(11):713. doi: 10.1038/s41574-022-00726-y
12. Rabinowitz JD, Enerbäck S. Lactate: the ugly duckling of energy metabolism. Nat Metab. 2020;2(7):566-71. doi: 10.1038/s42255-020-0243-4
13. Wender CL, Manninen M, O'Connor PJ. The Effect of Chronic Exercise on Energy and Fatigue States: A Systematic Review and Meta-Analysis of Randomized Trials. Front Psychol. 2022;13:907637. doi: 10.3389/fpsyg.2022.907637
14. Ranchordas MK, Rogerson D, Soltani H, Costello JT. Antioxidants for preventing and reducing muscle soreness after exercise: a Cochrane systematic review. Br J Sports Med. 2020;54(2):74-8. doi: 10.1136/bjsports-2018-099599
15. Engels RJ. The effect of delayed onset muscle soreness on jumping mechanics and performance [thesis]. South Dakota State University; 2017. Available from: https://openprairie.sdstate.edu/etd/1717
16. Vasconcelos SD, Salla RF. Resistance exercise, muscle damage and inflammatory response "what doesn't kill you makes you stronger". Sports Med. 2018;2(2):65-7. doi: 10.15406/mojsm.2018.02.00048
17. Cheung K, Hume PA, Maxwell L. Delayed onset muscle soreness: Treatment strategies and performance factors. Sports Med. 2003;33(2):145-64. doi: 10.2165/00007256-200333020-00005
18. Mizumura K, Taguchi T. Delayed onset muscle soreness: Involvement of neurotrophic factors. J Physiol Sci. 2016;66(1):43-52. doi: 10.1007/s12576-015-0397-0
19. Fonseca LB, Brito CJ, Silva RJ, Silva-Grigoletto ME, da Silva WM Junior, Franchini E. Use of cold-water immersion to reduce muscle damage and delayed-onset muscle soreness and preserve muscle power in jiu-jitsu athletes. J Athl Train. 2016;51(7):540-9. doi: 10.4085/1062-6050-51.9.01
20. Lima Rocha JÉ, Mendes Furtado M, Mello Neto RS, da Silva Mendes AV, Brito AK, Sena de Almeida JO, et al. Effects of Fish Oil Supplementation on

Oxidative Stress Biomarkers and Liver Damage in Hypercholesterolemic Rats. Nutrients. 2022;14(3):426. doi: 10.3390/nu14030426.
21. Yin Y, Wang J, Duan K, Cai H, Sun J. The effect of vibration training on delayed muscle soreness: A meta-analysis. Medicine (Baltimore). 2022;101(42):e31259. doi: 10.1097/MD.0000000000031259
22. Khataei T, Benson CJ. ASIC3 plays a protective role in DOMS through muscle acid sensation during exercise. Front Pain Res (Lausanne). 2023;4:1215197. doi: 10.3389/fpain.2023.121519
23. López-Ramírez O, González-Garrido A. The role of acid sensing ion channels in the cardiovascular function. Front Physiol. 2023;14:1194948. doi: 10.3389/fphys.2023.1194948
24. Corder KE, Newsham KR, McDaniel JL, Ezekiel UR, Weiss EP. Effects of Short-Term Docosahexaenoic Acid Supplementation on Markers of Inflammation after Eccentric Strength Exercise in Women. J Sports Sci Med. 2016;15(1):176-83.
25. Menzies P, Menzies C, McIntyre L, Paterson P, Wilson J, Kemi OJ. Blood lactate clearance during active recovery after an intense running bout depends on the intensity of the active recovery. J Sports Sci. 2010;28(9):975-82. doi : 10.1080/02640414.2010.481721
26. Gussoni M, Moretti S, Vezzoli A, Genitoni V, Giardini G, Balestra C, et al. Effects of electrical stimulation on delayed onset muscle soreness (DOMS): Evidences from laboratory and in-field studies. J Funct Morphol Kinesiol. 2023;8(4):146. doi: 10.3390/jfmk8040146
27. Huertas JR, Al Fazazi S, Hidalgo-Gutierrez A, López LC, Casuso RA. Antioxidant effect of exercise: Exploring the role of the mitochondrial complex I superassembly. Redox Biol. 2017;13:477-81. doi: 10.1016/j.redox.2017.07.009
28. Meng Q, Su CH. The Impact of physical exercise on oxidative and nitrosative stress: balancing the benefits and risks. Antioxidants (Basel). 2024;13(5):573. doi: 10.3390/antiox1305057
29. Belenichev I, Popazova O, Bukhtiyarova N, Savchenko D, Oksenych V, Kamyshnyi O. Modulating nitric oxide: implications for cytotoxicity and cytoprotection. Antioxidants (Basel). 2024;13(5):504. doi: 10.3390/antiox13050504
30. Lim AY, Chen YC, Hsu CC, Fu TC, Wang JS. The effects of exercise training on mitochondrial function in cardiovascular diseases: a systematic review and meta-analysis. Int J Mol Sci. 2022;23(20):12559. doi: 10.3390/ijms232012559
31. Salanova M, Schiffl G, Gutsmann M, Felsenberg D, Furlan S, Volpe P, et al. Nitrosative stress in human skeletal muscle attenuated by exercise countermeasure after chronic disuse. Redox Biol. 2013;1(1):514-26. doi: 10.1016/j.redox.2013.10.006
32. Deminice R, de Castro GS, Brosnan ME, Brosnan JT. Creatine supplementation as a possible new therapeutic approach for fatty liver disease: early findings. Amino Acids. 2016;48(8):1983-91. doi: 10.1007/s00726-016-2183-6
33. Clemente-Suárez VJ, Bustamante-Sanchez Á, Mielgo-Ayuso J, Martínez-Guardado I, Martín-Rodríguez A, Tornero-Aguilera JF. Antioxidants and sports performance. Nutrients. 2023;15(10):2371. doi: 10.3390/nu15102371
34. Gravina L, Ruiz F, Diaz E. Lekue JA, Badiola A, Irazusta J, et al. Influence of nutrient intake on antioxidant capacity, muscle damage and white blood cell count in female soccer players. J Int Soc Sports Nutr. 2012;9(1):32. doi: 10.1186/1550-2783-9-32
35. Ranchordas MK, Rogerson D, Soltani H, Costello JT. Antioxidants for preventing and reducing muscle soreness after exercise. Cochrane Database Syst Rev. 2017;12(12):CD009789. doi: 10.1002/14651858.CD009789.pub2
36. Clemente-Suárez VJ, Martín-Rodríguez A, Redondo-Flórez L, Ruisoto P, Navarro-Jiménez E, Ramos-Campo DJ, et al. Metabolic health, mitochondrial fitness, physical activity, and cancer. Cancers (Basel). 2023;15(3):814. doi: 10.3390/cancers15030814
37. Rhodes K, Braakhuis A. Performance and side effects of supplementation with N-acetylcysteine: A systematic review and meta-analysis. Sports Med. 2017;47(8):1619-36. doi: 10.1007/s40279-017-0677-3
38. Bielenichev IF, Gorchakova NA, Doroshenko EY, Samura IB, Ryzhenko VP, Bukhtiiarova NV. Use of metabolites, metabolithotropic agents and nutritional supplements in sports and sports medicine: a modern view on the problem. Modern Medical Technology. 2023;(4):76-88. 10.34287/MMT.4(59).2023.10
39. Bielenichev IF, Vizir VA, Mamchur VY, Kuriata OV. [Place of tiotriazoline in the gallery of modern metabolitotropic medicines]. Zaporozhye medical journal. 2019;21(1):118-28. doi: 10.14739/2310-1210.2019.1.155856
40. Kanda K, Sugama K, Hayashida H, Sakuma J, Kawakami Y, Miura S, et al. Eccentric exercise-induced delayed-onset muscle soreness and changes in markers of muscle damage and inflammation. Exerc Immunol Rev. 2013;19:72-85.
41. Pawłowska M, Mila-Kierzenkowska C. Effect of alpha-1 antitrypsin and irisin on post-exercise inflammatory response: a narrative review. Iran J Med Sci. 2024;49(4):205-18. doi: 10.30476/IJMS.2023.97480.2925
42. Meamarbashi A. Herbs and natural supplements in the prevention and treatment of delayed-onset muscle soreness. Avicenna J Phytomed. 2017;7(1):16-26.
43. Hsu CC, Tsai CC, Ko PY, Kwan TH, Liu MY, Wu PT, et al. Triptolide attenuates muscular inflammation and oxidative stress in a delayed-onset muscle soreness animal model. Int J Environ Res Public Health. 2022;19(24):16685. doi: 10.3390/ijerph192416685
44. Oku Y, Murakami K, Irie K, Hoseki J, Sakai Y. Synthesized Aβ42 caused intracellular oxidative damage, leading to cell death, via lysosome rupture. Cell Struct Funct. 2017;42(1):71-9. doi: 10.1247/csf.17006
45. Murase S., Terazawa E., Queme F. Ota H, Matsuda T, Hirate K, et al. Bradykinin and nerve growth factor play pivotal roles in muscular mechanical hyperalgesia after exercise (delayed-onset muscle soreness). J Neurosci. 2010;30(10):3752-61. doi: 10.1523/JNEUROSCI.3803-09.2010
46. Mizumura K, Taguchi T. Neurochemical mechanism of muscular pain: Insight from the study on delayed onset muscle soreness. J Physiol Sci. 2024;74(1):4. doi: 10.1186/s12576-023-00896-y
47. Gunina L. Implementation of the ergogenic action of antioxidative agents. Sporto Mokslas. 2015;81(3):2-10. doi: 10.15823/sm.2015.12
48. Köhne JL, Ormsbee MJ, McKune AJ. Supplementation strategies to reduce muscle damage and improve recovery following exercise in females: a systematic review. Sports. 2016;4(4):51. doi: 10.3390/sports4040051
49. Makaje N, Ruangthai R, Sae-Tan S. Effects of Omega-3 Supplementation on the Delayed Onset Muscle Soreness after Cycling High Intensity Interval Training in Overweight or Obese Males. J Sports Sci Med. 2024;23(2):317-25. doi: 10.52082/jssm.2024.317
50. Mackay J, Bowles E, Macgregor LJ, Prokopidis K, Campbell C, Barber E, et al. Fish oil supplementation fails to modulate indices of muscle damage and muscle repair during acute recovery from eccentric exercise in trained young males. Eur J Sport Sci. 2023;23(8):1666-76. doi: 10.1080/17461391.2023.2199282
51. Belenichev IF, Aliyeva OG, Popazova OO, Bukhtiyarova NV. Involvement of heat shock proteins HSP_{70} in the mechanisms of endogenous neuroprotection: the prospect of using HSP_{70} modulators. Front Cell Neurosci. 2023;17:1131683. doi: 10.3389/fncel.2023.1131683
52. Dos Santos RS, Veras FP, Ferreira DW, Sant'Anna MB, Lollo PCB, Cunha TM, et al. Involvement of the HSP_{70}/TLR4/IL-6 and TNF-α pathways in delayed-onset muscle soreness. J Neurochem. 2020;155(1):29-44. doi: 10.1111/jnc.15006
53. Costa-Beber LC, Heck TG, Fiorin PBG, Ludwig MS. HSP70 as a biomarker of the thin threshold between benefit and injury due to physical exercise when exposed to air pollution. Cell Stress Chaperones. 2021 Nov;26(6):889-915. doi: 10.1007/s12192-021-01241-1
54. Manojlović V, Erčulj F. Using blood lactate concentration to predict muscle damage and jump performance response to maximal stretch-shortening cycle exercise. J Sports Med Phys Fitness. 2019;59(4):581-6. doi: 10.23736/S0022-4707.18.08346-9
55. Akinci B, Zenginler Yazgan Y, Altinoluk T. The effectiveness of three different recovery methods on blood lactate, acute muscle performance, and delayed onset muscle soreness: a randomized comparative study. J Sports Med Phys Fitness. 2020;60(3):345-54. doi: 10.23736/S0022-4707.19.10142-9
56. Bischof K, Stafilidis S, Bundschuh L, Oesser S, Baca A, König D. Reduction in systemic muscle stress markers after exercise-induced muscle damage following concurrent training and supplementation with specific collagen peptides – a randomized controlled trial. Front Nutr. 2024;11:1384112. doi: 10.3389/fnut.2024.1384112
57. Souglis A, Bourdas DI, Gioldasis A, Ispirlidis I, Philippou A, Zacharakis E, et al. Time course of performance indexes, oxidative stress, inflammation, and muscle damage markers after a female futsal match. Sports (Basel). 2023;11(7):127. doi: 10.3390/sports11070127
58. Guest NS, VanDusseldorp TA, Nelson MT, Grgic J, Schoenfeld BJ, Jenkins ND, et al. International society of sports nutrition position stand: caffeine and exercise performance. J Int Soc Sports Nutr. 2021;18(1):1. doi: 10.1186/s12970-020-00383-4

59. Burke LM. Practical considerations for bicarbonate loading and sports performance. Nestle Nutr Inst Workshop Ser. 2013;75:15-26. doi: 10.1159/000345814
60. Che K, Yang Y, Zhang J, Feng L, Xie Y, Li Q, et al. Oral pyruvate prevents high-intensity interval exercise-induced metabolic acidosis in rats by promoting lactate dehydrogenase reaction. Front Nutr. 2023;10:1096986. doi: 10.3389/fnut.2023.1096986
61. Mora Carpio AL, Mora JI. Ventilator Management. [Updated 2023, Mar 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK448186/
62. Kyun S, Kim J, Hwang D, Jang I, Park HY, Lim K. Lactate administration induces skeletal muscle synthesis by influencing Akt/mTOR and MuRF1 in non-trained mice but not in trained mice. Physiol Rep. 2024;12(4):e15952. doi: 10.14814/phy2.15952