

Biochemical markers related to performance in women athletes

Marcadores bioquímicos relacionados à performance em mulheres atletas

Antônio Carlos Leal Cortez^{1,2} , Alexandrino Barbosa de Sousa Neto¹ , Antônio Carlos Gomes³ 

1. Centro Universitário Santo Agostinho (UNIFSA), Teresina, PI, Brazil

2. Laboratório de Biociências da Motricidade Humana – LABIMH-UNIRIO, RJ, Brazil

3. Centro Universitário Tereza D'ávila (UNIFATEA), Lorena, São Paulo, Brazil

ABSTRACT

Introduction: It is notorious that there are differences in relation to the biological composition between men and women, especially when we refer to physical performance, in which the morphological, physiological and biochemical characteristics are observed distinct between the sexes, even more, when it comes to the use of markers biochemicals related to the performance of female athletes. **Objective:** To elucidate the main biochemical markers that are related to performance in female athletes. **Methods:** The reflective theoretical path presented in this theoretical essay on health, outlined here on biochemical markers related to female performance, is based on a scientific literature review, as well as on national and international documents that addressed the issue in question. **Results:** The scientific evidence presented in the selected studies allowed us to present data regarding the anatomo-physiological effects of training on female athletes and on the main biochemical markers: Creatinokinase (CK), C-Reactive Protein, Lactate Dehydrogenase (LDH), Erythrocytes, Hematocrits, Hemoglobin, Testosterone, Estrogen, Progesterone, which suffer direct action according to the volume x training intensity, as well as the athlete's menstrual cycle. **Conclusion:** The scientific evidence presented during the study elucidated the main anatomo-physiological and biochemical differences between men and women and how they directly interfere, from the training process to performance, with no consensus on physiological parameters and specific biochemical markers for female athletes.

Keywords: female athlete; biomarkers; athletic performance.

RESUMO

Introdução: É notório que existem diferenças em relação à composição biológica entre homens e mulheres, principalmente quando nos referimos ao desempenho físico, no qual são observadas as características morfológicas, fisiológicas e bioquímicas distintas entre os sexos, ainda mais, quando se trata da utilização dos marcadores bioquímicos relacionados à performance das mulheres atletas. **Objetivo:** Elucidar os principais marcadores bioquímicos que estão relacionados à performance em mulheres atletas. **Métodos:** O percurso teórico reflexivo apresentado neste ensaio teórico em saúde, aqui delineado sobre os marcadores bioquímicos relacionados à performance feminina, pauta-se em revisão de literatura científica, bem como em documentos nacionais e internacionais que abordaram a temática em questão. **Resultados:** As evidências científicas apresentadas nos estudos selecionados nos permitiram apresentar dados referentes aos efeitos anátomo-fisiológicos do treinamento em mulheres atletas e sobre os principais marcadores bioquímicos: Creatinoquinase (CK), Proteína C Reativa, Lactato Desidrogenase (LDH), Eritrócitos, Hematócritos, Hemoglobina, Testosterona, Estrógeno, Progesterona, que sofrem ação direta de acordo com o volume x intensidade de treinamento, bem como com o ciclo menstrual da atleta. **Conclusão:** As evidências científicas apresentadas no decorrer do estudo elucidaram as principais diferenças anátomo-fisiológicas e bioquímicas entre homens e mulheres e como elas interferem diretamente, desde o processo de treinamento até a performance, não havendo consenso sobre parâmetros fisiológicos e de marcadores bioquímicos específicos para mulheres atletas.

Palavras-chave: mulher atleta; biomarcadores; desempenho atlético.

Introduction

From the moment that international sports bodies allowed the participation of female athletes in official sports competitions such as the 1924 Olympic Games in Paris/France, women began to participate more actively within the world sports scene in different sports. During all these years until today, women have been occupying more and more space in sports, even taking into account their anatomy and physiology and how their bodies and their biochemical reactions are expressed in the face of adaptations resulting from sports training [1].

It is clear that there are differences in relation to the biological composition between men and women, especially when we refer to physical performance, in which the physiological and morphological characteristics of men and women are observed. The different neuromuscular and metabolic responses between men and women reflect the action of characteristic hormones: testosterone for men and estrogen for women [2]. The action of these two substances directly influence cellular composition, with testosterone being directly linked to protein deposition in muscles, bones, skin and other parts of the body. Estrogen, on the other hand, is linked to increased fat deposition in the breasts, hips and subcutaneous tissue, which explains the greater amount of fat in females [3].

According to Fortes et al. [4], women have lower lean body mass, fewer sweat glands, a smaller heart, lower blood volume and lower concentrations of hemoglobin and hematocrit, which are factors that influence physical performance. Regarding lung function, there are also marked differences between the sexes, with men having a larger airway diameter, greater lung volumes and diffusion surfaces compared to adult women, which confers greater efficiency in performing the exercise. These sex differences in lung diffusing capacity are linked to the lower total number of alveoli (lower surface area) and smaller relative diameter of the airways in women [5].

It is important to emphasize that the physical and physiological adaptations are caused by physical training, within aspects of the principles of sports training, in this case the organism adapts to the stimuli, changing some parameters (physical, physiological, biochemical and biomechanical) such as muscle hypertrophy, gain lean mass, increased power (mainly aerobic), increased bone mineral density, increased number and size of mitochondria, increased glycogen storage, increased myofibrils, increased actin-myosin filaments, sarcoplasmic content, etc. [6].

The intensity and volume of training sessions, as well as the recovery time between sessions, have been a major concern for coaches, physiologists and sports scientists, as they are intervening factors in performance-oriented sports training, and there is a fine line among them. There are positive and negative consequences related to the stress of the training load, mainly for athletes who are always at the physical limits of their bodies. Therefore, we can describe these factors as overreaching and overtraining, which is the process that presents a drop in the physical performance of an athlete. The recovery from overreaching can take up to two weeks

and the recovery from overtraining can go from two weeks and take months [7,8].

Overtraining is caused by an imbalance between training stress and recovery. Athletes experience mental fatigue and a drop in performance. Overtraining has a great impact on the physiological and biochemical systems. We can mention as a consequence of this imbalance, in the physiological and biochemical systems, the decrease in muscle strength, coordination, increased perception of effort and recovery, changes in the lactate profile, sleep, anorexia, decrease also in muscle glycogen, bone mineral content, testosterone and testosterone/cortisol ratio above 30%, as well as increase in cortisol and urea [1,9-11].

Biochemical markers can be considered valid parameters to assess the occurrence of overtraining. This syndrome is accompanied by a marked response to oxidative stress biomarkers that are altered during high-intensity training and return to normal levels when the load is reduced, suggesting a dose-response relationship. Several direct and indirect methods have been used to analyze muscle damage from physical exercise. Indirect methods such as myoglobin, lactate dehydrogenase (LDH), myosin heavy chain fragment and CK are most commonly used [12].

These molecules can be used as markers of damage in skeletal muscle tissue due to the fact that they are cytoplasmic and thus impermeable in the plasmatic membrane. Thus, the increase in the levels of these molecules in the extracellular fluid may indicate a change in the permeability of the membrane or its disruption, thus causing loss of performance [13]. Thus, the study intends, through a theoretical essay in health, to describe the main biochemical markers that are related to performance in female athletes.

Methods

Methodological design

The study in question is a theoretical health essay, with a qualitative approach, aiming to bring a discussion, a new look and insights on issues of current interest [14].

Ethical care

The study was conducted in accordance with the Committee on Publication Ethics (COPE) guidelines, which contain information for authors and editors on research ethics [15].

Formulation of the research question

To guide the retrieval of information, the research question was structured aiming to guarantee not only the internal validity, but also the power of extrapolation of the results of the theoretical test. The scientific evidence of safety and efficacy is applicable among populations in different regions of the world and by the selection of studies in a comprehensive and exhaustive way, through the adoption of criteria

and evaluation of the quality and validity of the studies retrieved in the searches [16]. Thus, the aforementioned study has as its guiding question: What are the main biochemical markers that are related to performance in female athletes?

Definition of eligibility criteria

Inclusion and exclusion criteria for document selection are detailed in Chart 1.

Chart 1 - Description of inclusion and exclusion criteria for selection of studies

Inclusion	Studies in Portuguese, Spanish and English were included: randomized clinical trials, clinical studies, systematic review articles and other relevant scientific works that evaluated scientific evidence related to biochemical markers that are related to performance in female athletes
Exclusion	Publications that did not deal with the research object in question, studies with animals, studies that did not have published results, as well as studies that did not mention the conflict of interests were excluded.

Source: autores 2023

Selection of studies

The terms and interterms were defined from consultations, by the changed index, in DeCS, from which the descriptors in Portuguese and their respective MeSH were extracted, submitted to subsequent research to identify their interterms, in the databases Pubmed, Scielo, Web of Science and Scopus. The search for the definition of these terms and interterms was carried out in January 2023.

Strategies were listed to guide the identification and screening of studies. First, it was decided that the research period would be free to cover the largest volume of information. Second, the electronic search was carried out in the following databases: Pubmed, Scielo, Web of Science and Scopus. This choice was made to ensure greater coverage of peer-reviewed articles and to include a variety of journals with higher impact factors [17].

The keywords and Boolean operators chosen were “woman athlete”, “biochemical markers”, “performance”, using the Boolean operators AND/OR, as well as their synonyms, having as search scope the respective terms in the title, abstract and words of articles published in journals. This choice is due to a previous evaluation in the literature, in which the correlation between them and the frequency with which they are used in studies was verified.

Results e discussion

Therefore, the results presented by the theoretical essay in question propose a discussion based on scientific evidence, aiming to elucidate the anatomo-physiological effects of training and the main biochemical parameters for female athletes and, in this way, serve as a basis for future research on the subject, since there are still clinical gaps about the main biochemical markers that are related to performance in female athletes.

Thus, we chose to section the discussion of the theoretical essay addressing the following themes: anatomo-physiological effects of training in female athletes and biochemical markers in female athletes.

Anatomo-physiological effects of training in women athletes

In relation to structural and anatomical differences, women are 10 to 15 centimeters smaller than men, on average, and 10 to 20 kg lighter. The woman has a smaller muscle mass and, consequently, has a lower maximum strength, with lower tissue density, ligaments and muscles, which are more elastic and flexible [18].

According to cardiovascular dimensions, women have a smaller heart, lower blood volume and lower hemoglobin concentrations. Because her heart is smaller, end-diastolic volume, stroke volume, and cardiac output are smaller. Regarding the respiratory system, women have smaller nasal cavities, trachea, bronchi and lungs than men and smaller capillary volumes, resulting in lower pulmonary ventilation [19].

During aerobic exercises, a lower maximum oxygen consumption is observed in women compared to men, and the main hemodynamic mechanism involved is the lower cardiac output due to the lower systolic volume, a characteristic that, in turn, is consequent to the lower mass and volume ventricles in women, in addition, the oxygen-carrying capacity (due to a lower mean hemoglobin level resulting from menses) is lower in women [20].

Batlouni et al. [21] highlighted that during the transition from rest to exercise, systolic volume decreases more in women than in men, which explains why cardiac output, which is a product of systolic volume by heart rate, is directly related to Maximum VO_2 , therefore, the maximum consumption of oxygen is lower in females. Although adaptability to training is similar, these factors combine to cause women's athletic performance to be 6% to 15% lower than men.

Regarding flexibility, women's ligaments and muscles are more elastic and flexible, and through strength training, women's strength can be increased by about 20% to 40%. Because of estrogen's antioxidant effects, women have less muscle mass and less testosterone, which is very important in muscle hypertrophy, so there is less cell damage, but in terms of muscle fiber composition, they are similar and in women, the volume of each fiber, type I or type II, is greater than in men. These characteristics give men greater strength and muscular endurance than women [22].

Testosterone is considered a hormone that is related to the synthesis and reduction of muscle protein degradation. It is a predominantly male hormone, with anabolic and androgenic function, produced by Leydig cells in the testicles and also a small amount is secreted by the adrenal glands [23]. In women, the ovaries and adrenal glands are responsible for producing testosterone. Testosterone is more produced and released by males, which does justice to its function, greater muscle mass and characteristics such as more hair, deeper voice, sperm production, etc. Testosterone is also present in the female system in smaller amounts, and is dependent on glucocorticoid biosynthesis, in which the adrenal cortex secretes androgenic steroids that can be converted to testosterone [24].

The menstrual cycle influences a woman's performance. In the luteal phase, fat oxidation is greater and in the follicular phase, carbohydrate oxidation is greater. Catecholamines have more significant responses in the follicular phase [25]. Women use more fat as a source of substrate, therefore, blood glucose during exercise is higher than that of men, and carbohydrate consumption is lower in women [19].

The GH, also known as growth hormone or somatotropin, is the most abundant hormone secreted by the anterior pituitary, and there are two main genes involved in growth hormone synthesis: the normal GH gene expressed in the pituitary and the variant GH gene (GH-V or GH-2) expressed in the placenta, detectable in the circulation only during pregnancy or lactation, essential for a series of metabolic processes and growth of various tissues, including muscle [26,27].

During human development, GH secretion in both sexes reaches maximum concentrations during growth periods, mainly in adolescence, soon after that, both the frequency and the intensity of secretion are reduced, as for example an individual with about 20 years who secrete more than twice the amount of GH per day as older people. It should be noted that several factors can influence GH secretion, including nutritional status, amount of sleep and body fat, stress and physical activity or training level, etc. [28-31].

When we analyze the mechanism of action of GH in our body, we can describe it as an anabolic effect related to stimulating tissue growth and metabolism, altering the flow, oxidation and metabolism of almost all nutrients in circulation, which can be divided into direct and indirect effects. The direct effects are mediated by intracellular signaling cascades triggered by the binding of GH to its receptors on the plasmatic membrane, and the indirect effects are mediated mainly by the regulation of the synthesis of growth stimulated by physical exercise [27].

Many of the effects promoted by physical activity are affected by GH, including the reduction of protein catabolism and glucose oxidation, while increasing the mobilization of more FFAs (free fatty acids) in adipose tissue for energy production. These facts suggest that GH is an important hormone released in several stressful situations, however, studies have shown that GH also has anabolic effects, including promoting positive protein balance and increasing mass and IGF-1 release, involved in stimulating the muscular hypertrophy process [28,32,33].

Biochemical markers in women athletes

Biochemical markers can be considered significant parameters in evaluating the occurrence of overtraining. This syndrome is accompanied by a significant response of biomarkers of oxidative stress, which are altered during periods of intense training and return to normal levels when the load decreases, indicating a dose-response relationship, that is, volume x intensity of training. Many direct and indirect methods have been used in the analysis of muscle damage resulting from physical exercise [12,35].

Indirect methods such as myoglobin, lactate dehydrogenase (LDH), myosin heavy chain fragment, and CK are most commonly used. These molecules can be used as markers of skeletal muscle tissue injury because they are cytoplasmic and therefore cannot penetrate the plasma membrane. Therefore, increased levels of these molecules in the extracellular fluid may indicate changes in membrane permeability or membrane rupture [13,36].

CK plays a key role in muscle cell energy formation, as it is an enzyme within the muscle responsible for maintaining adequate ATP levels during muscle contractions. It is known that the use of this marker to control the training load and the diagnosis of overtraining is still under discussion, and that changes in CK activity after exercise vary with different exercise conditions, clinical evaluation of induced muscle damage the exercise is very difficult. But CK can be a marker of fatigue and overload in non-athletes [11]

Prolonged and vigorous physical exercise increases CK levels, and the magnitude of this increase is directly related to the intensity and duration of the activity. It is believed that the effects of prolonged continuous exercise can trigger mechanisms that induce CK extravasation into the blood, where CK measurements seem to be sensitive and reliable parameters to assess the increase in muscle stress or exercise tolerance in individuals. The total CK value above 500UI/L has been used as a parameter to indicate damage to the muscle tissue [37,38].

In athletes, the study of CK at rest and after exercise can be an important tool for technicians and physicians. Athletes have higher levels of CK at rest when compared to untrained individuals, probably due to greater muscle mass and daily synthesis, however, after exercise, serum CK activity depends on the athlete's training level, although athletes have greater muscle soreness when compared to untrained individuals, the peak serum activity is lower [39].

Serum CK concentration peaks 1 to 4 days after exercise and remains elevated for several days. Thus, athletes who participate in daily training have higher resting values than non-athletes, although this response to training is attenuated by the so-called repeated attack effect, that is, the repetition of an exercise after several days or even weeks causes less damage to muscle fibers than that caused by the previous exercise [40].

For athletes, the reference interval for CK is different for each gender, with the upper reference limit for men being more than twice as high as for women; in addition, it is in agreement with the existence of reference intervals for the Sex-specific CK in the general population. These differences can be explained by the higher amount of CK in male muscle than in female muscle, although other factors such as muscle membrane permeability, CK clearance rate and lymphatic activity cannot be excluded [40,41].

According to Hecksteden et al. [42], CK is an important marker related to muscle recovery and muscle soreness, being essential in adjusting the daily physical training load. In this case, we must take into account when evaluating this bio-

chemical marker, the individual differences of each athlete in relation to the group, performing individualized reference intervals in order to optimize the monitoring of muscle recovery.

In addition to CK, we also have LDH (lactate dehydrogenase), an enzyme present in cells that is responsible for glucose metabolism in the body. This enzyme can be found in various organs and tissues, so its elevation is not very specific and requires additional tests to make a diagnosis, and usually, its elevation indicates organ or tissue damage. This is because, as a result of cellular damage, intracellular LDH is released and circulates in the blood, and its concentration is assessed by blood tests [43]. It is worth noting that several factors influence the increase in CK and LDH after physical exercise, such as age, sex, type of exercise performed, physical conditioning and the volume x intensity of exercise performed [44,45].

Another important biochemical marker in the process of assessing muscle wasting is C-reactive protein (CRP), which is a protein synthesized by the liver. Its levels increase in response to inflammation, so it is a reactive protein in the acute phase of training, having interleukin-6 (IL-6) as the main inducer, which influences the protein transcription process during the acute phase of an inflammatory or infectious process. An important role played by PCR is the recognition of pathogens or damaged cells [46].

In acute conditions of physical exercise, CRP concentrations increase during the first 6 to 8 hours after inflammation or tissue injury, and may reach up to thousands of times above the normal level in approximately 48 hours. CRP is a clinical marker of great value due to its analytical stability, in addition to showing reproducible results, high sensitivity and good precision [47,48].

Together with the markers mentioned above, we have the analysis of the red series, which include the quantification of erythrocytes (RBCs), hematocrit, hemoglobin dosage and hematimetric indices (VCM, HCM, CHCM, RDW), as well as the microscopic examination of the erythrocyte morphology. These sets of analyzes provide subsidies for the diagnosis of the main causes of anemia [49].

It is worth emphasizing that the biochemical markers have differences in their classifications in view of sex, since there are anatomo-physiological differences that cause the concentrations of these markers to vary greatly, taking into account aspects such as the menstrual cycle and body composition [50]. In chart 2, we present the main biochemical markers related to the performance of female athletes.

Chart 2 - Main biochemical markers related to the performance of female athletes

Biochemical marker	Reference values
Creatine kinase (CK)	29.00 U/L to 168.00 U/L
C-Reactive Protein	Very high risk: above 10 mg/L or 1 mg/dL High risk: 2.0 mg/L or 0.2 mg/dL Medium risk: between 1.0 and 2.0 mg/L or 0.1 and 0.2 mg/dL Low risk: less than 1.0 mg/L or 0.1 mg/dL
Lactate Dehydrogenase (LDH)	230.0 to 460.0 U/L
Erythrocytes	3.9 to 5.3 M/mm ³
Hematocrit	35 to 45%
Hemoglobin	Non-pregnant state: 12 to 16 g/dL Pregnant women: 11 g/dL
Testosterone	Age between 16 and 21 years old: 17.55 – 50.41 ng/dL Over 21 years old: 12.09 – 59.46 ng/dL During menopause: up to 48.93 ng/dL
Estrogen	Follicular phase: 50.0 to 100.0 pg/mL Luteal phase: 100.0 to 300.0 pg/mL Menopause: 10.0 to 60.0 pg/mL
Progesterona	Onset of menses: 1 ng/mL or less Before ovulation: less than 10 ng/mL 7 to 10 days after ovulation: greater than 10 ng/mL In the middle of the menstrual cycle (ovulation): 5 to 20 ng/mL First trimester of pregnancy: 11 to 90 ng/mL Second trimester of pregnancy: 25 to 90 ng/mL Third trimester of pregnancy: 42 to 48 ng/mL

Fonte: Cortez, Sousa Neto e Gomes (2023)

Conclusion

With the increase in the number of women participating in different sports and with the advancement of sports science, we can then analyze, with more biological parameters, the physiological and biochemical differences between male and female athletes and how they interfere with performance. These differences, presented in the study in general, do affect the female performance in relation to the male. Factors such as a smaller heart, smaller ejection volume, smaller number of pulmonary alveoli, as well as a smaller production of testosterone - a hormone directly related to the lean mass gain, a very important variable within performance -, in addition to other hormonal changes caused by the menstrual cycle, among others, make women have different physiological and biochemical responses.

The scientific evidence presented during the study described the main anatomophysiological and biochemical differences between men and women and how they directly interfere, from the performance process in the training system to performance. Therefore, the application of biochemical markers is of great importance

throughout the process, emphasizing that they must be used together and during all phases of training, to be more reliable in their results, in addition to creating biochemical parameters, in order to avoid overtraining and loss of performance.

Another important fact is that there is no consensus on physiological parameters and specific biochemical markers for female athletes, and these variables are extremely important for physiologists and sports coaches. Thus, it is necessary to monitor exercise physiologists throughout the training process, creating an information system aimed at evaluating each athlete separately, respecting their biological individualities, aiming to create their specific physiological and biochemical parameters, avoiding overtraining and performance loss. Thus, we conclude the need for the development of experimental research that addresses the theme in question, in order to establish physiological and biochemical parameters aimed at female athletes, aiming at monitoring the training action, mainly related to the biochemical markers that directly reveal their effects on the body female referring to training actions and competitions in which they participate.

Conflict of interest

The authors report that there are no conflicts of interest

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Authors' contribution

Research conception and design: Cortez ACL, Sousa Neto AB, Gomes AC; **Data analysis and interpretation:** Cortez ACL, Sousa Neto AB; **Statistical analysis:** Cortez ACL, Sousa Neto AB; **Writing of the manuscript:** Cortez ACL, Sousa Neto AB, Gomes AC; **Critical review of the manuscript for important intellectual content:** Cortez ACL, Gomes AC.

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