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CARBOXYTHERAPY AS DOPING IN ATHLETES

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Abstract

Athletic achievements are impossible without significant physical activity during training and competitions, which puts forward extremely high requirements for the body. Therefore, today sport cannot do without the pharmacology possibilities. For many years there are prohibited pharmacological substances (doping) that artificially increase physical performance, endurance and, as a result, the effectiveness of competitions, thereby creating a dishonest advantage of the athlete over rivals. A safe and effective, and most importantly not prohibited, alternative to existing doping substances is the use of carbon dioxide - non-invasive (baths, inhalation) and invasive (subcutaneous or intradermal CO_2 injection) carboxytherapy. Any methodological option for the use of carboxytherapy (invasive or non-invasive) in different sequences and intensities activates the same mechanisms of self-regulation, leading to the restoration of homeostasis: improving the function of external respiration and synchronously with this autoregulation of vascular tone. Increasing blood flow and normalizing the rheological properties of blood eliminates venous stagnation, mobilizes anaerobic (reserve) energy exchange and reduces oxygen consumption by the heart muscle. Improvement of tissue oxygenation and trophy stimulates neovascularization, metabolism and collagen formation and accelerates reparative processes and excretion of lactic acid. As a result, there is a rapid restoration of impaired performance, physical endurance of athletes and an increase in their tolerance to excessive physical activity. Carboxytherapy is a simple and safe procedure. The safety and non-toxicity of medical CO_2 usability guaranteed by the use of carboxytherapy system, certified in Europe and Ukraine and justifies the possibility of using carboxytherapy in sports medicine as a safe and effective alternative to doping

Keywords: *carbon dioxide, carboxytherapy, athletes, doping.*

Athletic achievements are impossible without significant physical activity during training and competitions, which puts forward extremely high requirements for the body. Which create a constant need to find and implement means to increase and restore physical performance to prevent athlete overload. Therefore, today sport cannot do without the pharmacology possibilities. For many years there are prohibited pharmacological substances (doping) that artificially increase physical performance, endurance and, as a result, the effectiveness of competitions, thereby creating a dishonest advantage of the athlete over rivals [1, 2, 3].

Control over doping absence is entrusted to the World Anti-Doping Agency (WADA; World Anti-Doping Agency - WADA), which defines and controls substances and methods prohibited for use in sports. The list of doping substances is an international standard that regulates substances and methods prohibited in sports. The list also lists substances and methods prohibited for use in certain sports. Each year, WADA publishes a new version of the list with an updated list of prohibited substances [4].

Prohibited substances primarily include androgens, anabolic steroids and their analogues, peptide hormones, growth factors and their analogues, β2-agonists (β2-adrenomimetics), hormone antagonists, metabolism modulators, diuretics and masking agents, CNS stimulants and alcohol. Prohibited methods include manipulation of blood and its components, chemical and physical manipulations, gene doping [5].

Contrary to the listed prohibited substances and methods, there are pharmacological drugs - non-doping drugs - the use of which in athletes is not limited. Unlike doping, these drugs do not cause an excessive unproductive increase in physical endurance, performance and do not create an artificial advantage for the athlete in comparison with athletes who do not take these drugs. Non-doping drugs for use in sports medicine are not intended to enhance or suppress certain biochemical, biophysical or physiological reactions, but exclusively to modulate them and create favorable metabolic and homeostatic conditions for adaptation and realization of the athlete's existing potential, without artificially increasing it [6].

A safe and effective, and most importantly not prohibited, alternative to existing doping substances is the use of carbon dioxide - non-invasive (baths, inhalation) and invasive (subcutaneous or intradermal CO_2 injection) carboxytherapy. All cells of the body (neurons, hepatocytes, cardiomyocytes, chondrocytes, epithelial cells, etc.), regardless of the functions performed, emit CO_2 as the product of the biochemical reactions of their vital activity [7, 8].

Today, carboxytherapy is an innovative direction in medicine for the different disease's treatment, since it is capable to influence on an extensive set of pathological symptoms, which impact explains by the multifunctional participation of CO_2 in many metabolic and reflex processes of systemic self-regulation of the body. CO_2 acts as an intermediary that triggers cascades of natural regulation mechanisms in all body systems (respiratory, transport, nervous, cardiovascular, excretory, hematopoietic, immune, humoral, etc.). All these vital systems of the body play an important role in maintaining its homeostasis. With a low level of CO_2 and bicarbonates in the blood, the body ceases to function normally and the cascade of natural biochemical reactions in order to restore homeostasis becomes ineffective [9, 10, 11, 12].

The body simultaneously undergoes many biochemical processes with a catabolic or anabolic orientation. The result of catabolic reactions is the loss of carbon by the body through the breakdown of carbon bonds and the release of this element from the body in the form of CO_2. The main manifestation of anabolic reactions, on the contrary, is the processes of carbon accumulation. The carboxylation process takes one of the central places in the metabolism and carbon cycle in the biosphere. More than 20 carboxylation reactions discovered in various microorganisms, as well as in tissues of animals and humans. Consequently, the rate of CO_2 accumulation serves as an indicator of the anabolic potential of the organism, while the rate of oxygen consumption indicates the intensity of catabolic oxidative processes [13].

The ratio of CO_2 and O_2 in the body characterizes the dominant direction of metabolic processes towards dissimilation or assimilation. An increase in the intensity of carboxylation processes accompanied by an increase in the synthesis of

organic compounds, and a decrease in CO_2 levels can cause inhibition of anabolism in the body [9].

Thus, the entire path of a person from birth to death represents a process of progressive reduction in CO_2 utilization and an increase in dependence on O_2 consumption to compensate for a reduced carbon dioxide reserve. At the same time, the body's own contribution to the processes of maintaining the energy balance increases sharply, independent of the external environment, and recycle relations between the intensity of CO_2 formation and the rate of O_2 consumption are formed. Metabolism in the body carried out with the participation of aerobic and anaerobic processes. The aerobic metabolism process in the body is associated with the use of oxygen. The resistance of newborns to oxygen deficiency is 8-10 times higher than in adults [7].

If chemical reactions take place without oxygen, such processes called anaerobic. Aerobic processes in humans are basic, and anaerobic processes are auxiliary or reserve, and almost constantly accompany aerobic processes. In everyday life, we do work within 35% of our absolute capabilities, work in the range of 35-50% of absolute capabilities leads to fatigue, and above 65% of absolute capabilities lies the "mobilization threshold." Only protected autonomous body reserves remain outside this border. Anaerobic-type reactions lead to oxygen starvation and the accumulation of under-oxidized metabolic products in tissues: for example, lactic and pyruvic acids, which cause a pain reaction in muscles, limit the ability of the body to use the mechanism of "second breathing.» However, the gradual use of the anaerobic type of breathing leads the body to changes in the internal environment, which increases its resistance to adverse factors. If with intensive skeletal muscle work, aerobic processes increase tenfold and then anaerobic processes increase hundreds of times as the body's natural strategic reserve. Under these conditions, the physiological concentration of CO_2 in cells is necessary for the normal course of all biochemical processes [14, 15, 16].

The role of CO_2 as a natural stimulator of respiration is that with the slightest change in its concentration (by 0.1%), numerous mechanisms are included to quickly return the concentration of CO_2 to the physiological norm, since the body is a self-healing and self-regulating system.

Carbon dioxide is the most important product of cellular respiration, so there are many sensors in the body that regulate its concentration. Therefore, CO_2 level shift from physiological values turns on numerous mechanisms of adaptation, which are in detail described in the section physiological CO_2 value in any party. The increase in CO_2 concentration is a signal for increasing the intensity of respiration and circulation, reducing tension and muscle spasm, which contributes to analgesic and anti-inflammatory effects, increasing the body's resistance to adverse factors [17].

In hypoxia, occurring against the excessive physical exertion. Due to the inclusion of reserve anaerobic respiration as an effective means of obtaining energy during short periods of intense tension (when the delivery of oxygen to the muscles is insufficient to maintain aerobic metabolism), under-oxidized exchange products, in particular lactic and pyruvic acids, accumulate in the muscles of athletes, which cause a pain reaction. Under such conditions, carboxytherapy due to the elimination of hypoxia leads to a decrease in the formation of lactic acid, eliminating pain [18, 19].

However, the ability of carboxytherapy to affect a large pathological symptoms explains by the participation of CO_2 in many metabolic and reflex processes of systemic self-regulation. Since CO_2 acts as a biochemical pacemaker, signaling molecule, triggering the cascades of the above mechanisms in all body systems (respiratory, nervous, cardiovascular, excretory, hematopoietic, immune, humoral, etc.) and plays an important role in maintaining homeostasis.

Since carbon dioxide is a physiological stimulator of respiration, a mixture of O_2 (93-95%) and CO_2 (5-7%) called carbogen (non-invasive carboxytherapy) is used in medical practice. With inhalation of carbogen in a healthy person, the breathing volume increases by 5-7 times. The stimulating effect of CO_2 on breathing develops within the first 5-6 minutes. This improves both general and cerebral blood circulation.

Another example of non-invasive carboxytherapy is the V.K. Buteiko method - a complex of respiratory exercises. The effectiveness of this method verified in a number of randomized clinical

trials. Method V.K. Buteyko proposes correction of breathing due to reduction of frequency and amplitude of respiratory movements: slow shallow breathing with delays of inhalation and exhalation acts leads to accumulation of CO2 in blood and realization of its effects (antihypoxant, antioxidant, vasodilator, etc.). There is no negative effect on the volume of pulmonary respiration and other systems of the body using the V.K. Buteiko method [20, 21].

Carbon dioxide baths as an example of non-invasive carboxytherapy are useful not only for patients, but also for healthy people to strengthen the body with large physical and nervous loads, to increase the body's resistance to adverse environmental factors. Carbon dioxide baths are widely used in sports medicine. When taken an hour after or 3 hours before training, carbon dioxide baths increase the tone of the nervous, respiratory and cardiovascular systems, improve metabolism, accelerate the excretion of lactic acid, which contributes to faster recovery from physical activity [22].

CO2 enhances metabolism in the brain, increases mental performance and has a unique effect of eliminating subcortical congestive foci of arousal, since under the influence of CO2 nerve excitability reduces. At the point of CO2 injection the sensitivity of nerve endings changes, tissue trophy improves and local protective processes intensified. Due to antioxidant impact of CO2 on the body resistance to adverse environmental factors is increased.

A doctor, who has completed a special course or training and has a corresponding certificate, can perform Carboxytherapy. After the course of treatment, the same doctor observes the patient. You should inform the doctor about all medications taken before and after the procedure, as well as in cases of any signs of allergy [23].

There are no specific indications after performing the injection carboxytherapy, but it is desirable not to wet the injection site during the first 4 hours. Avoid sharp temperature differences within 2 days after the session: do not visit the sauna, bath, do not take hot baths, do not visit the solarium, do not hypothermia.

Targeted patients for carboxytherapy are adults. After injection in a certain area of the body, you cannot immediately wear underwear with a tightening effect.

Motor activity will only improve the effects of CO2, so there is no need to change the lifestyle.

The use of carbon dioxide to stimulate breathing should done with great care. Insufficient ventilation of the lungs created when breathing weakened and can lead to an accumulation of CO2 in the body and cause poisoning.

On the day of the procedure, it is advisable to drink a lot of liquid, better non-carbonated and unsweetened water or tea.

Before carboxytherapy, fatty creams should not use and not be exposed to UV radiation for a long time. It is undesirable to come to the procedure immediately after physical exertion, after sports (long cycling, etc.), in a state of stress.

The procedure does not require any special rehabilitation regime.

The course of treatment requires 5-20 sessions, between which there can be certain intervals established by the doctor individually for each patient. The duration of the first procedure should not exceed 5-7 minutes. During the procedure of carbon dioxide baths, it is necessary to constantly monitor the pulse (a slowdown in the pulse is a sign of good tolerance of the bath, an increase in the pulse rate is sometimes a signal to stop the procedure) [20].

To prevent excessive amount of CO2 from entering the patient's body through the respiratory organs, which is collected above the surface of the water during the carbon dioxide bath procedure, it is advisable to cover the mineral gas bath with a wet sheet. With "dry" carbon dioxide baths, the cutout of the bag around the patient's neck is compacted so that heat and gas do not go out. The filling of bags with CO2 begins after they fixed in the waist or neck area.

After the mineral-gas and "dry" carbon dioxide bath, the patient wipes with a heated sheet.

It is better to take a carbon dioxide bath after rest, 30-40 minutes after a light breakfast. The effectiveness of treatment increased if the baths taken at the same time.

The patient should immerse slowly in the bath to prevent the release of CO2 and reduce its concentration in the mixed water. During the procedure, for better layering of gas bubbles on the skin, the patient should lie calm, not move.

After carbon dioxide baths, the patient can use body cream or milk to prevent dry skin.

To mitigate the adaptation process after the procedure recommended resting for 15-60 minutes.

Forbidden to take carbon dioxide baths if the patient drank alcohol or potent drugs, as the threat of heart failure increases.

Also forbidden to use electrical appliances at a distance of not less than 1.5 meters from the bath.

During the 70-year history of carboxytherapy, including almost 50 years of use in the practice of aesthetic and traditional medicine, there are no serious side effects. The risk of infection in carboxytherapy is minimized by the use of sterile gas (and bactericidal properties of CO_2) and high-tech equipment.

The above mechanisms of action of CO_2 make it possible to use widely carboxytherapy in sports medicine in conditions accompanied by hypoxia and tissue ischemia, fatigue and reduced physical performance [24].

Any methodological option for the use of carboxytherapy (invasive or non-invasive) in different sequences and intensities activates the same mechanisms of self-regulation, leading to the restoration of homeostasis: improving the function of external respiration and synchronously with this autoregulation of vascular tone. Increasing blood flow and normalizing the rheological properties of blood eliminates venous stagnation, mobilizes anaerobic (reserve) energy exchange and reduces oxygen consumption by the heart muscle. Improvement of tissue oxygenation and trophy stimulates neovascularization, metabolism and collagen formation and accelerates reparative processes and excretion of lactic acid. As a result, there is a rapid restoration of impaired performance, physical endurance of athletes and an increase in their tolerance to excessive physical activity. Carboxytherapy is a simple and safe procedure. The safety and non-toxicity of medical CO_2 usability guaranteed by the use of carboxytherapy system, certified in Europe and Ukraine and justifies the possibility of using carboxytherapy in sports medicine as a safe and effective alternative to doping

References

1. Mudrak J, Slepicka P, Slepickova I. Sport motivation and doping in adolescent athletes. PLoS One. 2018 Oct 4;13(10):e0205222. doi: 10.1371/journal.pone.0205222. PMID: 30286200; PMCID: PMC6171920.
2. Tlili R, Zayed S, Saoudi W, Azaiez F, Hentati R, Ben Ameur Y. Adverse cardiovascular effects of doping in athletes. Tunis Med. 2019 Nov;97(11):1211-1218. PMID: 32173820.
3. Palmi I, Berretta P, Tini A, Ricci G, Marinelli S. The unethicality of doping in sports. Clin Ter. 2019 Mar-Apr;170(2):e100-e101. doi: 10.7417/CT.2019.2117. PMID: 30993304.
4. Aguilar-Navarro M, Salinero JJ, Muñoz-Guerra J, Plata MDM, Del Coso J. Sport-Specific Use of Doping Substances: Analysis of World Anti-Doping Agency Doping Control Tests between 2014 and 2017. Subst Use Misuse. 2020;55(8):1361-1369. doi: 10.1080/10826084.2020.1741640. Epub 2020 Mar 18. PMID: 32186429.
5. Houghton E, Maynard S. Some aspects of doping and medication control in equine sports. Handb Exp Pharmacol. 2010;(195):369-409. doi: 10.1007/978-3-540-79088-4_17. PMID: 20020374.
6. Kondric M, Sekulic D, Petroczi A, Ostojic L, Rodek J, Ostojic Z. Is there a danger for myopia in anti-doping education? Comparative analysis of substance use and misuse in Olympic racket sports calls for a broader approach. Subst Abuse Treat Prev Policy. 2011 Oct 11;6:27. doi: 10.1186/1747-597X-6-27. PMID: 21988896; PMCID: PMC3204239.
7. The antioxidant action of CO_2 - one of the universal mechanisms of carboxytherapy / Drogovoz S. M., Kalko K. O., Ivantsyk L. B., Shtroblya A. L., Stoletov Yu. V., Drogovoz K. V., Ostasko V. F. Pharmacologyonline. 2021. Vol. 2. P. 158-166. https://pharmacologyonline.silae.it/files/archives/2021/vol2/PhOL_2021_2_A019_Drogovoz.pdf

8. Carboxytherapy as an alternative off lable method for diabetes mellitus treatment: a review / Drogovoz S. M., Kalko K. O., Hailat I. A., Ivantsyk L. B., Kireyev I. V. Pharmacologyonline. Vol. 3. 2021. P. 447-455.
9. Bunyatyan ND, Drogovoz SM, Kononenko AV, Prokofiev AB. Karboksiterapiia - odno iz innovatsionnykh napravleniĭ v kurortologii [Carboxytherapy - an innovative trend in resort medicine]. Vopr Kurortol Fizioter Lech Fiz Kult. 2018;95(5):72-76. Russian. doi: 10.17116/kurort20189505172. PMID: 30412151.
10. El-Domyati M, Hosam El-Din W, Medhat W, Ibrahim MR, Khaled Y. Carboxytherapy for striae distensae: A promising modality. J Cosmet Dermatol. 2021 Feb;20(2):546-553. doi: 10.1111/jocd.13844. Epub 2020 Dec 3. PMID: 33205585.
11. Oliveira SMD, Rocha LB, da Cunha MTR, Cintra MMM, Pinheiro NM, Mendonça AC. Effects of carboxytherapy on skin laxity. J Cosmet Dermatol. 2020 Nov;19(11):3007-3013. doi: 10.1111/jocd.13337. Epub 2020 Feb 24. PMID: 32091181.
12. Abdel Kareem IM, Fouad MA, Ibrahim MK. Effectiveness of subcision using carboxytherapy plus fractional carbon dioxide laser resurfacing in the treatment of atrophic acne scars: comparative split face study. J Dermatolog Treat. 2020 May;31(3):296-299. doi: 10.1080/09546634.2019.1595505. Epub 2019 Apr 2. PMID: 30889369.
13. Benner A, Lewallen NF, Sharma S. Physiology, Carbon Dioxide Response Curve. 2021 Jul 23. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan–. PMID: 30844173.
14. Anderson CT, Breen PH. Carbon dioxide kinetics and capnography during critical care. Crit Care. 2000;4(4):207-15. doi: 10.1186/cc696. Epub 2000 Jul 12. PMID: 11094503; PMCID: PMC150038.
15. Morales Quinteros L, Bringué Roque J, Kaufman D, Artigas Raventós A. Importance of carbon dioxide in the critical patient: Implications at the cellular and clinical levels. Med Intensiva (Engl Ed). 2019 May;43(4):234-242. English, Spanish. doi: 10.1016/j.medin.2018.01.005. Epub 2018 Feb 24. PMID: 29486904.
16. Martin WF. Carbon-Metal Bonds: Rare and Primordial in Metabolism. Trends Biochem Sci. 2019 Sep;44(9):807-818. doi: 10.1016/j.tibs.2019.04.010. PMID: 31104860.
17. Wimmer Z, Zarevúcka M. A review on the effects of supercritical carbon dioxide on enzyme activity. Int J Mol Sci. 2010 Jan 19;11(1):233-53. doi: 10.3390/ijms11010233. PMID: 20162013; PMCID: PMC2821001.
18. Julu POO, Shah M, Monro JA, Puri BK. Carbon dioxide therapy in hypocapnic respiratory failure. Med Hypotheses. 2018 Jan; 110: 101-104. doi: 10.1016 / j.mehy.2017.11.010. Epub 2017 Dec 2. PMID: 29317050.
19. Experience and prospects of carboxytherapy in diabetes mellitus / S. M. Drogovoz, G. V. Belik, K. O. Kalko, S. I. Shevchenko, L. V. Derymedvid, I. V. Kireyev, A. L. Shtroblya. Problems of Endocrine Pathology. No. 4. 2021. P. 110-116.
20. Carboxytherapy as one of the innovative directions in balneology / S. M. Drogovoz, N. D. Bunyatyan [et al.] // Issues of balneology, physiotherapy, and physical therapy. - 2018. - Vol. 95. - No. 5. P. 72–76.
21. Nesek-Adam V, Mrsić V, Smiljanić A, Oberhofer D, Grizelj-Stojcić E. Patofizioloski ucinci CO2-pneumoperitoneja u laparoskopskoj kirurgiji [Pathophysiologic effects of CO2-pneumoperitoneum in laparoscopic surgery]. Acta Med Croatica. 2007 Apr; 61 (2): 165-70. Croatian. PMID: 17585472.
22. Matsumoto T, Tanaka M, Ikeji T, Maeshige N, Sakai Y, Akisue T, Kondo H, Ishihara A, Fujino H. Application of transcutaneous carbon dioxide improves capillary regression of skeletal muscle in hyperglycemia. J Physiol Sci. 2019 Mar;69(2):317-326. doi: 10.1007/s12576-018-0648-y. Epub 2018 Nov 26. PMID: 30478742.
23. Smith KJ, Wildfong KW, Hoiland RL, Harper M, Lewis NC, Pool A, Smith SL, Kuca T, Foster GE, Ainslie PN. Role of CO2 in the cerebral hyperemic response to incremental

normoxic and hyperoxic exercise. J Appl Physiol (1985). 2016 Apr 15;120(8):843-54. doi: 10.1152/japplphysiol.00490.2015. Epub 2016 Jan 14. PMID: 26769951; PMCID: PMC4835911.

24. Kanazawa M, Sugama S, Okada J, Miura M. Pharmacological properties of the CO2/H+-sensitive area in the ventral medullary surface assessed by the effects of chemical stimulation on respiration. J Auton Nerv Syst. 1998 Aug 6;72(1):24-33. doi: 10.1016/s0165-1838(98)00085-x. PMID: 9760077.