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THE VERSATILITY OF CARBOXYTHERAPY IN PATHOGENIC THERAPY

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Abstract

Carbon dioxide is a powerful physiological regulator (physiological and pharmacological pacemaker) of numerous body systems: cardiovascular, respiratory, nervous, excretory, hematopoietic, immune, etc. Therefore, at present, carboxytherapy, due to the universal nature of pharmacodynamics, its physiology is one of the methods widely used in medicine for the treatment of a large number of diseases and has received official recognition in many countries worldwide. The use of CO_2 in surgery is not limited to disinfection of surgical wounds, wound healing, anti-inflammatory, hemostatic and antioxidant effects. Inhaling carbon dioxide in a low concentration (3-5%) has a reflex stimulating effect on the respiratory and vasomotor centers of the medulla oblongata: it causes deep and rapid breathing, and excitation of the vasomotor center - an increase in heart rate and blood pressure. This reflex effect of CO_2 is used during anesthesia to stimulate pulmonary ventilation with a mixture of CO_2 and O_2 (carbogen) while suppressing pulmonary ventilation. Inhalation of CO_2 helps with vascular collapse to increase cerebral blood flow. Thus, carboxytherapy in the complex of pharmacotherapeutic treatment of diseases is a worthy alternative to drugs that have synergistic pathogenetic (antioxidant, antihypoxic, anti-inflammatory) and symptomatic (vasodilator, analgesic, hypolipidemic, antiseptic, reparative) effects.

Keywords: *carbon dioxide, carboxytherapy, pathogenic therapy.*

Carbon dioxide is a powerful physiological regulator (physiological and pharmacological pacemaker) of numerous body systems: cardiovascular, respiratory, nervous, excretory, hematopoietic, immune, etc. Therefore, at present, carboxytherapy, due to the universal nature of pharmacodynamics, its physiology is one of the methods widely used in medicine for the treatment of a large number of diseases and has received official recognition in many countries worldwide [8,9,12,20,21,29,37,48].

In recent decades, the positive effects of invasive carboxytherapy have been widely used in diseases of the musculoskeletal system, especially for solving problems and during the recovery period after injuries of the joints and spine [14, 38,25]. Today, in many recreational and medical facilities of the world, carboxytherapy is a non-surgical method of treating diseases of the spine and joints [8,49]. About a third of the world's population suffers from various disorders of the musculoskeletal system. First of all, carboxytherapy is used for joint diseases that are poorly amenable to therapy by other traditional methods. Course use of invasive carboxytherapy in orthopedics allows consolidating a positive therapeutic effect for a long time in the treatment of osteochondrosis, arthritis, arthrosis, synovitis, gout, and other joint diseases [16]. Carboxytherapy is used to eliminate inflammation, chronic joint and muscle pain, and restore joint function. The main targets of carboxytherapy in orthopedics are Zakharyin-Ged hyperesthesia zones, trigger points, myofibralgia zones, and acupuncture points. Due to the listed effects of carboxytherapy, stiffness in the joint area is eliminated and it is especially effective in the first and second phases of the pathological process in the joints (with desynchronization and functional disorders) [13]. Its analgesic effect is noticeable already at the "tip of the needle" and further extends to all parts of the musculoskeletal system: from exteroceptors, trigger, and acupuncture points, to joints, muscles, ligaments, and bone tissue itself.

In invasive carboxytherapy, medical CO_2 is injected directly into the tissue around the joint, which suffers from hypoxia, ischemia, and inflammation. The central nervous system, having received a signal from a local injection of CO_2 in the joint area, reflexively stimulates the flow of oxygen-enriched blood to the joint, resulting in pronounced local oxygenation, hyperemia of the periarticular bursa, and after 10-15 minutes the pain syndrome is relieved. Under the action of carboxytherapy, hypoxia, spasm, ischemia, muscle tension, stiffness are reduced, congestion (lymphatic and venous swellings) is eliminated, and also due to the rather pronounced antioxidant and anti-inflammatory effect of CO_2, the functions of the spine and joints are restored [47,40,31]. In chronic inflammatory and degenerative diseases of the joints, CO_2, acting on these reflexogenic zones, affects not only the musculoskeletal system but many internal organs.

Consequently, CO_2 injections around the joints, due to the reflex multifactorial impulse action, cause a decrease in the tone of terminal arterioles and capillaries, improve the oxygenation of the joints, change the activity of nerve endings, and, due to vasodilation and relaxation of muscle fibers, lead to an improvement in joint trophism, antispasmodic, analgesic and anti-inflammatory effects. [50, 32, 41].

A common cause of pain is myofascial syndrome, in which the analgesic and antispasmodic effect of CO_2 is achieved through changes in the sensitivity of nerve endings, vasodilation, and relaxation of muscle fibers [26]. The mechanism of invasive CO_2 administration involves not only its effect on neurotransmission but there are other positive components. When CO_2 is administered intradermally, it irritates the nociceptors, thereby stimulating them to release endorphins. In addition, the CO_2 injection itself is a mild nociceptive signal (causing "physiological pain") [51,35].

Therefore, by acting purposefully on the tissues in the area of administration, carbon dioxide increases blood flow, providing analgesic, anti-inflammatory, antispasmodic and antioxidant effects. Changes in the activity of nerve endings (in response to changes in pH in the joints), vasodilation, relaxation of muscle fibers at the site of CO_2 injection improve tissue trophism. Carbon dioxide administered during carboxytherapy is excreted from the body within 30 minutes by the lungs and kidneys, and the processes launched by it in the body, including in the joints, slow down only by the end of 2-3 weeks [8,47].

In addition, the resorptive analgesic effect of CO_2 in the body includes the main mechanisms of adaptation of homeostasis: a neurohumoral response with the inclusion of the hypothalamic-

pituitary system of endogenous pain regulation and the ability to optimize antinociceptive self-regulation (stimulation of endogenous synthesis of endorphins, which provide an analgesic effect). The analgesic effect of carbon dioxide injections is associated not only with the synthesis of endorphins but also with the improvement of tissue trophism at the site of local action of CO_2. With muscle tension, CO_2 has a beneficial effect on pain points. In this case, the placebo effect also plays an important role: the release of endorphins and the placebo effect are in close synergism during carboxytherapy [28,33].

Thus, an important role in the mechanism of action of carboxytherapy belongs to the neurohumoral and reflex influence of CO_2, which is carried out at the local, segmental, suprasegmental levels with the participation of the somatic and autonomic parts of the peripheral nervous system, subcortical-stem formations, and the cerebral cortex.

The use of carboxytherapy in dermatology and cosmetology is also associated with the local and resorptive effects of CO_2. Non-invasive carboxytherapy (baths, cosmetic masks, gels, and creams) has a pharmacological effect due to the ability of CO_2 to penetrate well through the skin due to its high amphiphilicity [11]. During carboxytherapy at the injection site of CO_2, a state of local hypercapnia occurs, which causes vasodilation, the flow of oxygen-enriched blood, increased metabolic processes, an increase in the rate of cell regeneration (fat burning, enhanced synthesis of collagen, elastin, and hyaluronic acid), improved lymphatic drainage and removal of intercellular fluid, reduction of inflammatory processes of the skin and the beginning of the processes of regeneration of skin cells (rejuvenation) [22].

As a result of the local action of CO_2 in the skin, the intensity of blood flow, cell proliferation, and the course of immune and inflammatory reactions change. In addition, subcutaneous injection of CO_2 stimulates fibroblasts, and this, in turn, has a positive effect on the processes of neocollagenogenesis, which is one of the important mechanisms of skin rejuvenation. Involvement of the deeper layers of the skin leads to a long and constant production of collagen and, as a result, to a general tightening of the skin of the face: eyelids, cheeks, and neck. The most pronounced aesthetic result of carboxytherapy is based on these mechanisms: the elasticity of the skin is increased, its flabbiness is eliminated [23 52,,18].

Consequently, the mechanism of action of carboxytherapy in cosmetology is realized simultaneously in several directions: carbon dioxide saturating the tissues stimulates blood circulation and increases the release of oxygen, and with the help of oxyhemoglobin, tissues receive a powerful stimulus for regeneration. Under the action of carboxytherapy, platelets release factors present in alpha granules, which help to accelerate the repair and regeneration of endothelial cells. After several sessions of carboxytherapy, the subcutaneous tissue is restructured: fibrous adhesions are destroyed, tissue homogeneity is achieved [34,17].

In turn, with stretch marks in the lower eyelids, carboxytherapy stimulates the formation of collagen and reduces the volume of subcutaneous fat (there is a "compression" of the connective tissue frame). The same principle of the mechanism of action of carboxytherapy occurs with cicatricial tissue, scars, and traces of acne. The presence of carbon dioxide in the tissues leads to an intensive supply of oxygen from the bloodstream to the tissues. This stimulates red blood cells to deliver larger amounts of oxygen to cells, as well as metabolic processes. Within 30 minutes after the injection, the injected carbon dioxide is eliminated from the body, and at the injection site, the blood vessels expand, the blood flow increases, which stimulates the cell to function in a new mode: metabolic processes are accelerated, and toxins are actively eliminated. CO_2 initiates the formation of biologically active substances and collagen in the skin, which leads to regeneration, accelerated tissue healing, and renewal [3].

The action of CO_2 in cellulite is also associated with its positive microcirculatory effect on the altered network of microarteries, veins, and lymphatic vessels that cross the connective tissue [53]. With a dosed invasive administration of carbon dioxide, the body, quickly responding to an increase in its concentration, increases blood and lymph circulation at the site of CO_2 injection, toxic metabolites begin to be actively eliminated, swelling decreases, and lipolysis and oxygenation processes intensify. In the process of carboxytherapy, CO_2

enters the subcutaneous fatty tissue under pressure, which contributes to the mechanical destruction of fat cells, and also changes the acidity of the latter, and accelerates lipid peroxidation. Lipid vacuoles freed from adipocytes are eliminated by macrophages. Diffusely distributed in the subcutaneous tissue, CO_2 causes vasodilation, which eliminates the stagnation of lymph and venous blood in the tissues and improves the elimination of toxins. Expansion of blood vessels and increased blood circulation in the subcutaneous tissue leads to an increase in the process of lipolysis - the natural process of breaking down fat. Under the influence of carboxytherapy, the sensitivity of β2- andβ3-adrenergic receptors to adrenaline increases, which leads to an increase in the natural process of lipolysis (in fat cells, β2- and β3-adrenergic receptors predominate). In addition, CO_2 is directly involved in lipid hydrolysis in adipose tissue by activating cAMP, which in turn stimulates hormone-dependent lipase. It is also assumed that the anti-cellulite mechanism of action of CO_2 is associated with hypercapnia (Verigo-Bohr effect). This has a positive effect on physiological oxidative and lipolytic processes, and activation of blood circulation promotes oxygenation of subcutaneous fat, which also improves the process of lipolysis and removal of toxins [19,30,45].

As can be seen from the above, the mechanisms of action of carboxytherapy are diverse and are associated with the active stimulation of reparative and metabolic processes in tissues: CO_2 promotes tissue oxygenation; biochemical processes dependent on the latter, associated with the proliferation of fibroblasts and the function of protective mechanisms, increase. Along with solving local problems, CO_2 has a systemic effect on the body: muscle relaxant, analgesic, anti-inflammatory, antioxidant, rheological, and the increased level of tissue oxygenation improves tissue trophism and the protective properties of the body. The resorptive action of CO_2 starts from the exteroreceptors at the tip of the needle and ends with the internal organs. Consequently, carboxytherapy not only eliminates muscle-vascular spasm, relieves myofascial pain syndrome, eliminates venous-interstitial lymphatic stasis, improves tissue trophism, but also promotes detoxification processes, increases local skin immunity and tissue regeneration [45].

It follows from this that carboxytherapy activates basic defense mechanisms, facilitating the transition of the body to more beneficial ways of maintaining metabolism. As a result, all types of metabolism (carbohydrate, fat, protein, electrolyte), reparative, and metabolic processes in organs are enhanced. By restoring oxygenation and enhancing metabolic processes at the cellular level, fibroblasts are stimulated, which produce not only elastin and hyaluronic acid, but also collagen and interferons, and the function of the latter is associated with specific receptors on the cell surface. As a result, complex intracellular signaling mechanisms are activated with the onset of rapid activation of gene transcription. Genes stimulated by interferons modulate powerful physiological and biochemical effects that are important for the resistance of cells affected by viruses. In addition, interferons stimulate the production of cortisol, which has an anti-inflammatory effect [8].

Consequently, the ability of carboxytherapy to affect an extensive pathological symptom complex can be explained by the participation of CO_2 in many metabolic and reflex processes of systemic self-regulation, that is, CO_2 acts as a biochemical pacemaker that triggers cascades of the above-described mechanisms of all body systems (respiratory, transport, nervous, cardiovascular, excretory, hematopoietic, immune, humoral, etc.) and plays an important physiological role in maintaining homeostasis [47].

Subcutaneous injections of CO_2 induce local mild alkalosis, which promotes analgesic and antispasmodic action; local hyperemia, oxygenation, which are accompanied by bactericidal (especially for aerobic microorganisms) and anti-inflammatory action. At the same time, tissue perfusion is improved due to vascular dilatation, reparative and metabolic processes are enhanced, and receptor sensitivity is restored. The tissue in the area of the CO_2 injection receives a powerful stimulus for regeneration and, as a result, the tissues are restructured after just a few carboxytherapy procedures [8].

The same pharmacotherapeutic principles of carboxytherapy are used to treat diabetic foot [12,21,43,44]. Increasing the delivery of CO_2 to the

ulcerated area increases the release of nitric oxide, which leads to an increase in oxygen content and blood flow to the ulcerated foot tissue. Improved angiogenesis and oxygenation promote ulcer healing (anti-inflammatory, reparative action). Simultaneously with the activation of blood circulation and the enhancement of metabolic processes at the site of the administration of carbon dioxide, the function of skin fibroblasts is stimulated, which affects the synthesis of collagen, elastin, and hyaluronic acid. It is these three components that are responsible for the condition of the skin and other tissues: the more there are, the better the skin looks. Fibroblasts, in addition to the formation of collagen, are producers of interferons, which are involved in providing bactericidal and anti-inflammatory effects [12, 21].

The mechanisms of carboxytherapy are associated with the peculiarities of the ways of using carbon dioxide, so during the procedure of a "dry" carbon dioxide bath, CO_2 freely penetrates the body in two ways: with inhaled air and through the skin, as a result, its content in the blood increases, blood vessels dilate, oxygenation, neoangiogenesis, neocollagenogenesis, immunity, regeneration processes are stimulated, inflammation, irritability, fatigue decrease. At the same time, there is an improvement in the blood supply to the skin, muscles, and internal organs. Inhalation of CO_2 leads to increased breathing, as a result of which the lungs are more oxygenated [21].

The physiotherapeutic effects of CO_2 in balneology (the effect of aqueous and "dry" carbon dioxide baths) can be explained by the combined effect of thermal, mechanical, chemical, and reflex factors. The thermal factor of carbon dioxide baths is realized due to a pronounced reflex-irritating effect on the heat receptors of the skin, a decrease in the activity of cold receptors, and an increase in skin blood flow until the patient feels warm. The mechanical action (tactile massage) of carbon dioxide baths is associated with irritation of the skin baroreceptors with CO_2 bubbles. Thermal and mechanical factors of carbon dioxide baths activate a cascade of positive reflex and neurohumoral processes. So, during the first hours after taking a bath, all patients note lightness and vigor. Penetrating the body through the lungs, carbon dioxide affects the respiratory center, slowing down and deepening breathing [26].

The biochemical effect of carbon dioxide baths is due to the fact that during their administration, carbon dioxide penetrates the body with the inhaled air and through the skin, as a result of which its content in the blood increases and a cascade of the above-described effects appears, which improves oxygenation, vasodilation, vascularization and energy supply of all organs and body tissues [8]. CO_2-containing beverages, irritating the taste buds of the oral cavity and chemoreceptors of the gastric mucosa due to mechanical and chemical action, reflexively increase appetite, stimulate the formation of hydrochloric acid and enzymes, absorbing, digesting, and motor activity of the gastrointestinal tract [47].

Thus, due to the polypathogenetic pharmacodynamics of carbon dioxide, carboxytherapy is an effective and safe method of treating many diseases, therefore today it is difficult to name a branch of medicine where the pharmacological properties of CO_2 are not used and carboxytherapy would not receive confirmation of its efficacy and safety [8, 9,12,20,21,29,37,48].

In clinical neurological practice, the effectiveness of injectable carboxytherapy for encephalopathy, atherosclerosis, Meniere's syndrome, neuritis, neurasthenia, dizziness of various origins, post-stroke hemiparesis, other types of paresis, and the consequences of cerebrovascular accident, migraine, sleep disorders, Parkinson's disease, vegetative-vascular dystonia, polyneuropathies, and postherpetic neuralgia is noted [46,1]. The effect of pain reduction is especially evident after the first procedures of invasive apparatus and non-invasive carboxytherapy for headaches associated with vestibular tension, migraine, chronic discirculatory ischemia and encephalopathy, arachnoiditis, intracranial hypertension, and vertebrogenic pain syndromes. In meteorological people with headaches, when using invasive carboxytherapy, there is a feeling of relief and an increase in mental performance without the use of analgesics. The ability of carboxytherapy to relieve pain allows its use in the treatment of these neurological diseases. In this case, carboxytherapy, in addition to the above effects, also has an anti-inflammatory effect, eliminates muscle-vascular spasms, relieves

myofascial pain syndrome, eliminates venous congestion, and reduces the number of analgesics used. The therapeutic effects of carboxytherapy in neurology are achieved due to the antihypoxic, anti-ischemic, anti-inflammatory, analgesic, antispasmodic and antioxidant properties of CO2. However, this procedure is empirical, complementary, and is not considered a substitute for any other neurological treatment [5,28,48].

Marketing analysis indicates that carboxytherapy has found effective application in many fields of medicine, but especially a great deal of experience in its application has been accumulated in cosmetology and dermatology. Today carboxytherapy is an innovative modern method with the help of which aesthetic medicine achieves high results. CO2 therapy can be used to solve many cosmetic problems: when signs of skin aging appear, for body shaping during liposuction (before and after the procedure), for eliminating many cosmetic defects (stretch marks, scars, dark circles, wrinkles with lipodystrophy (cellulite)), and other skin pathologies, and also to protect the body from harmful physical and chemical factors. To rejuvenate the skin of the face and body, the most commonly used effects of carboxytherapy are vasodilation, oxygenation, and rapid restoration of the balance of intradermal collagen, elastin, and hyaluronic acid. The result of carboxytherapy does not take long to see and is clearly visible after 2 procedures or within the next 7-14 days. But for the correction of the shape of the lower eyelid, the fight against a double chin, as well as for rejuvenation, more carboxytherapy procedures and time are required. At a young age, an alternative to invasive carboxytherapy, as well as a good addition to enhance the result, can be the use of carboxy gel masks [39].

Consequently, carboxytherapy in cosmetology and aesthetic dermatology allows solving skin problems of various etiologies caused by hypoxia, quantitative and qualitative impairment of collagen fibers, vascularization processes, regeneration, and restoration of the aesthetic appearance of the skin [42].

Recently, carboxytherapy has become popular in the West for the treatment of lipid dystrophy (cellulitis). Carboxytherapy is a widely used procedure for all stages of cellulite. A large clinical experience accumulated over 50 years has confirmed that carboxytherapy is a very effective procedure in the fight against lipodystrophy and local obesity. It provides mechanical destruction of fatty deposits due to CO2 pressure on them, elimination of lymph congestion, and, as a result, elimination of toxins. When assessing the local effect of carboxytherapy on adipose tissue, the positive effect of CO2 on the process of oxidative lipolysis has been established. Also, carboxytherapy is prescribed after liposuction to eliminate skin relief. Only 10-15 sessions make the skin smooth and taut [7].

CO2 therapy in dermatology is indicated for the treatment of such skin diseases: limited neurodermatitis, acne, focal scleroderma, psoriasis, eczema, cicatricial tissue of various origins, allergic dermatoses, as well as for improving blood circulation, enhancing the protective properties of the skin, faster healing of wounds (diabetic, ischemic, postoperative and post-traumatic), burns, ulcers, reduction of itching of the skin, allergic reactions and inflammatory processes. Trophic ulcers and keloid scars (with complicated diabetes mellitus) respond well to treatment with carboxytherapy. By enhancing the processes of oxygenation and regeneration, as well as the antibacterial properties of CO2, the healing and smoothing of the skin are accelerated [2, 27,4,24].

Carboxytherapy is used to treat psoriasis, a chronic autoimmune skin disease characterized by red, white and gray papules, hyperkeratosis, cracks, and sometimes pustules. The effects of CO2 in this pathology are achieved by improving local vascularization, oxygenation with the administration of CO2, as well as its anti-inflammatory, antiallergic, antihypoxic, antioxidant, regenerating, analgesic, and antimicrobial effects. In cosmetology and dermatology, CO2 gas injections are combined with mesotherapy, lipolytic mesotherapy, chemical peeling, hardware rejuvenation (photothermolysis and deencrustation), since CO2 greatly enhances their action due to the synergistic effects. In addition, several times fewer procedures are required [6, 10].

The use of CO2 in surgery is not limited to disinfection of surgical wounds, wound healing, anti-inflammatory, hemostatic and antioxidant effects. Inhaling carbon dioxide in a low concentration (3-

5%) has a reflex stimulating effect on the respiratory and vasomotor centers of the medulla oblongata: it causes deep and rapid breathing, and excitation of the vasomotor center - an increase in heart rate and blood pressure. This reflex effect of CO2 is used during anesthesia to stimulate pulmonary ventilation with a mixture of CO2 and O2 (carbogen) while suppressing pulmonary ventilation [9, 29]. Inhalation of CO2 helps with vascular collapse to increase cerebral blood flow.

Thus, carboxytherapy in the complex of pharmacotherapeutic treatment of diseases is a worthy alternative to drugs that have synergistic pathogenetic (antioxidant, antihypoxic, anti-inflammatory) and symptomatic (vasodilator, analgesic, hypolipidemic, antiseptic, reparative) effects.

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