



Carboxytherapy Non-Invasive Method in Dermatology and Some Other Branches of Medicine

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Abstract

The 21st century is an era of cutting-edge technologies and unique discoveries, including carboxytherapy, which is one of the most universal and widely used innovative medical technologies that emerged at the end of the 20th century and quickly came to life. Today, it is difficult to name an area of medicine where carboxytherapy doesn't have an "excellent" efficacy and safety assessment. However, what unfairly remains a "white spot" on the map of carboxytherapy is the lack of information about it in textbooks, catalogues, journals, as well as a lack of theoretical justification of the mechanism of action and the indications for its use in medical forms and treatment protocols.

Keywords: Carboxytherapy; Dermatology; Medicine

Introduction

In current medicine there is an unlimited portfolio of diagnostics tools and therapeutic modalities to treat various conditions. The utilisation of CO₂ gas has a long tradition in many branches of medicine, be it in form of systemic (inhalation) or local (transdermal, intradermal, subdermal, and intramuscular) therapy. The term "carboxytherapy" today denotes predominantly the utilisation of CO₂ gas in injection form.

Carboxytherapy – therapeutically applied carbon dioxide injections have been used in balneotherapy since 1932, thanks to the balneotherapists from the French Royat Spa. Since then, the number of publications dealing with carboxytherapy has been increasing every year, advocating the great effects of this therapeutic modality. In balneotherapy, the said "gas injections" are applied predominantly to treat joint problems and impaired blood circulation in the lower extremities (ischemic disease) and in the skin of diabetic patients, but also in some patients with systemic vascular diseases and diseases of the heart (bradycardia, low blood pressure) [1,2,8,12,15,17,18,20,23,24]. In the last two years, however, this treatment modality has become the centre of attention as a unique method applicable in dermatology, aesthetic dermatology and anti-aging medicine [1,3-6,11-17,20,21,23-34].

Characteristics of CO₂

Carbon dioxide is a colourless, inflammable, mostly non-reactive gas heavier than air. It is a product of biological processes, for

example of respiration of all aerobic organisms and fermentation, combustion of wood, carbohydrates and fossil fuels such as coal, peat, petroleum and natural gas. Under normal pressure it occurs in form of gas, while its instable solid form is referred to as dry ice. Carbon dioxide is a common compound of atmosphere, whereby its concentration (CO₂ gas measurements) in atmosphere oscillates depending on local conditions, altitude, and relative air humidity. Due to especially industrial emissions, its average concentration in the air keeps growing [8,10,19].

CO₂ and its transport in bodily tissues

Physiologically, the human body produces approximately 1.0 kg of CO₂ a day, which contains 290 g of carbon. CO₂ is transported by the venous system (high content CO₂) and exhaled by the lungs (low content CO₂). The arterial system shows only a low concentration. The content of CO₂ in blood is also referred to as arterial carbon dioxide partial pressure.

Mechanism of action of CO₂ due to the Bohr effect

The Bohr effect is a physiological phenomenon first described in 1904 by the Danish physiologist Christian Bohr, stating that haemoglobin's oxygen binding affinity is inversely related both to acidity and to the concentration of carbon dioxide. An increase in blood CO₂ concentration which leads to a decrease in blood pH will result in haemoglobin proteins releasing their load of oxygen. Conversely, a decrease in carbon dioxide provokes an increase in pH, which results in haemoglobin picking up more oxygen. Since carbon dioxide

reacts with water to form carbonic acid, an increase in CO₂ results in a decrease in blood pH. $HbO_2 + H^+ \rightleftharpoons O_2 + HHb^+$

Major physiological effects of carbon dioxide

One of the major physiological effects of carbon dioxide is its stimulatory effect on the chemoreceptors of the respiratory and vasomotor centres of medulla oblongata. As a result, breathing is enhanced and accelerated, including improved tissue respiration, coronary dilatation, increased stroke volume and cardiac output, reduced myocardial and CNS ischemia. Stimulated immunogenesis and repair processes in inflammation-affected area, as well as better mental performance are observed. This means that in physiological concentration, CO₂ is necessary for the normal functioning of the human body, due to regulation of cellular respiration, maintenance of homeostasis and acid-base equilibrium, angiogenesis, and immunity. Carbon dioxide baths stimulate the synthesis of testosterone and estradiol, and are used with success to treat sexual dysfunction in men (erectile dysfunction) and to alleviate the symptoms of menopause in women.

Immune system	Increases the body’s resistance to adverse environmental factors by preventing cell damage via active oxygen forms (antioxidant effect)
Digestive system	Enhances the function of digestive glands (salivary glands, liver) as well as gastric mucous membranes that produce hydrochloric acid
Urinary system	Relieves convulsive spasms of the urinary bladder, accelerates diuresis
Endocrine and reproductive system	Stimulates the secretion of pancreatic hormones (bicarbonates stimulate insulin secretion by pancreatic cells) and sexual glands (bicarbonates stimulate the synthesis of testosterone and estradiol); Strengthens metabolic processes in the body: carbohydrates, fats, proteins, electrolytes.

Table 1: Physiological role of CO₂ in safeguarding the functioning of the systems of the human body (elaborated according to Prof. Drogovoz S.M).

System	Role of CO ₂
Respiratory system	Stimulating effect on chemoreceptors in the respiratory centre of medulla oblongata
Circulatory and lymphatic system	Stimulating effect on chemoreceptors of the vasomotor centre of medulla oblongata, direct vasodilant effect; Enhances circulation of blood and lymph, reduces swelling, helps eliminate metabolic waste; Promotes faster release of oxygen from haemoglobin bonds; Increases vascular endothelial growth factor that stimulates neoangiogenesis, regulates blood viscosity; Plays a role in the buffer system of the human body (the ph of blood plasma depends on the ratio of bicarbonate to dissolved carbon dioxide concentration)
Nervous system	Participates in the distribution of sodium ions, regulates nerve cell excitability, helps reduce cerebral cortex stagnation
Cosmetic effects (skin and mucous membranes)	Accelerates elimination of toxins, repair, and neoangiogenesis
Musculoskeletal system (bones, joints, muscles, ligaments)	Relieves muscle spasms, minimizes sensitivity to pain, accelerates elimination of toxins

General indications of carboxytherapy

Carboxytherapy is currently being used with success in many branches of medicine, including:

- Orthopaedic medicine and physiotherapy to manage pain, condition after traumas, arthritis, acute and chronic back pain and pain in other areas (due to the hypoalgetic effect of medicinal CO₂)
- Neurology to manage patients after encephalitis, Parkinson’s disease, vegetative dystonia, or polyneuropathy
- Gynaecology to treat oligomenorrhea and amenorrhoea
- Urology to manage erectile dysfunction associated with microangiopathy
- Rheumatology to reduce painful muscle irritation
- Angiology, phlebology, diabetology to improve blood circulation in tissues in acrocyanosis, Raynaud’s disease, Buerger’s disease, or arteriopathy
- Wound healing in chronic venous insufficiency with lower leg ulcerations, diabetic wounds (accelerated healing)
- Sports medicine
- Balneology
- Lymphology to improve oedema
- Surgery to accelerate healing after skin implants, carpal tunnel surgery, Dupuytren’s contracture
- Psychiatry to manage panic attacks and foster convalescence and regeneration in persons with carcinoma, neu-

tralise the negative effects of irradiation and chemotherapy, induce euphoria, accelerate mental regeneration (positive motivation)

- Dermatology to treat alopecia (alopecia areata, partially also alopecia androgenetica), small localised psoriatic foci, morphaea, keloid and burn scars, stretch marks, lichen ruber planus and hypertrophicus, onychorrhexis (by different authors with limited results achieved so far)
- Aesthetic medicine and aesthetic dermatology to improve skin elasticity, in anti-ageing therapy to promote rejuvenation, smooth out wrinkles on the face, neck, and lower neck, tighten lax skin on the chin, arms, abdomen, in body contouring after liposuction, lipolysis or other aesthetic procedures, and to treat cellulite (which can be improved but not completely reduced, however, some authors report that carboxytherapy prevented the development of cellulite), and to reduce oedema and dark circles under the eyes

General contraindications of carboxytherapy

The general contraindications of carboxytherapy include severe ischemic heart disease, acute embolism, thrombophlebitis and phlebothrombosis, gangrene, renal failure, untreated high pressure, stroke, pregnancy, lactation, severe adiposity with a BMI above 25 (body contouring), acute infectious disease, fever, excessive blood clotting, usage of anti-coagulants, hysteria, or fear of needles.

Other contraindications also include high expectations and high biological age of the patient.

On the day of carboxytherapy administration the patient must not be diagnosed with an acute infectious disease or infectious inflammatory skin disease such as impetigo, herpes simplex or herpes zoster, have increased body temperature or fever.

Devices used in carboxytherapy

Many older devices are being modernised, and many companies strive to make them as small as possible. The small handy devices look like pens (Carboxy Pens- small handy devices) and allow for continuous administration. Their advantages is size, however, they often are too heavy to be held in one hand during longer sessions. The devices used in carboxytherapy of course had to pass through this development and on the market there are multiple variants, ranging from the so called "pens" to sophisticated devices featuring displays with detailed information.

Regulations and requirements related to CO₂ gas administration in medicine

The regulations are very strict, medicinal CO₂ gas is only supplied by licensed companies. The CO₂ gas used in carboxytherapy devices must be sterile, must not contain more than 1% oxygen,

must not contain more than 4% nitrogen, must contain more than 95% CO₂, and must be chemically and biologically harmless.

CO₂ gas administration techniques and modalities

In general, they differ based on the projected and desired treatment result and depend on the erudition of the expert administering carboxytherapy to skin, subcutaneous tissue, muscles, joints, and spinal area. The technique used to administer CO₂ abides by certain rules. There are two types of administration (used in the treatment of carboxytherapy) and each of them has its advocates and opponents. Many centres use devices adjusted according to purpose, whereby the gas applied either way will spread in adjacent tissues, the variable being the administration time [7- 9,29].

Continuous administration and bolus administration of CO₂

Continuous administration is a technique of gradual administration of a predefined amount of CO₂ in certain localities (intra-dermal administration), under the skin (subdermal administration) and into deeper structures (subcutis, fatty tissue, muscles in physiotherapy and neurology, fibrous tissue in keloid scars or in Morbus Peyronie, etc.). Continuous administration is preferred by some experts also when treating the face, neck, and décolletage. The disadvantage is the longer injection interval and the risk of unwanted movement of the inserted needle (especially with pens, which may be small but quite heavy and come with a small cartridge placed in the handle). The amount of CO₂ gradually fills in the treated areas.

Bolus administration of CO₂ is the administration of certain predefined bolus doses of CO₂ into predefined localities. The session takes less time and is more comfortable for the patient, especially when treating more extensive or sensitive localities.

Intra-dermal and intra-cutaneous administration of CO₂ gas

This type of superficial administration results in visible lifting of the tissue, especially when targeted at skin imperfections and uneven appearance, and here the needle is inserted at the angle of 15 to 30 degrees.

Subcutaneous (subdermal) administration of CO₂ gas

The administration is deeper, the angle of the needle is 45 degrees and CO₂ is administered in an antegrade manner.

Intra-muscular or on fat deposits administration of CO₂ gas

Intra-muscular CO₂ gas injections are given perpendicular to the skin at the angle of the needle of 90 degrees.

Injection administration of CO₂ gas in acupuncture points

Also called pneumopuncture, the administration of minimum doses (max. 5 ml/minute) of medicinal CO₂ to acupuncture points potentiates the effect of acupuncture by stimulating certain

(hyperalgetic) points on the skin. The administration of CO₂ gas (via a complex neurohumoral mechanism) has an analgesic effect in algic syndromes of varying aetiology, and a positive influence on muscle tone, due to which it is used in neurological indications – parietic conditions and other indications [16,19].

Novelties in application

Innovations and the ability to use multiple puncture technique (for example in injection lipolysis) play a very important role, since boluses of CO₂ are applied in exact distances of approximately 1 cm and the dose is increased depending on the expected effect of individual injections.

Recommended length of needles used in carboxytherapy

The needles used are usually 30G mesotherapy needles, where by the selected length depends on the erudition of the physician, for example:

To treat skin laxity, stretch marks on abdomen and lower abdomen, knees, and cellulite the recommended length of the needle is 12 to 13 mm.

To treat the face, wrinkle, dark circles under the eyes, hand dorsae, atrophic scars, neck, and lower neck the recommended length of the needle is 4 to 6 mm.

The needle should be replaced after 8 to 10 injections and it is necessary to consider the sensitivity of the individual patient, as in very sensitive patients local anaesthesia (gels with content of Lidocain) or cooling (cold packs, or Ice Cooler® Pro) is recommended, the needle must be replaced more often, and the flow CO₂ should be decreased.

General recommendations for patients undergoing carboxytherapy

Before carboxytherapy: for at least 3 days adhere to a proper drinking regimen (drink 2-3 l/day). In case you undergo treatment of locomotive organs or cellulite, we recommend you bring comfortable clothing with you. If you undergo the treatment of skin and subcutaneous tissue, consult your physician and ask about adequate cosmetics. Your physician must be informed of any and all used drugs as well as any allergies.

After carboxytherapy: on the day of administration and 3 to 5 days after the procedure it is inevitable to increase the intake of liquids such as still water and tea. If undesired sensations occur, contact your physician.

It is necessary to abide by the above rules, stick to a well balanced diet, refrain from smoking and drinking alcohol, and exercise. It is also good to refrain from overusing analgesic drugs.

Undesired effects during the treatment session

The injection pain (due to nociception) is minimal, controlled, and resolves within a few seconds. A crackling sensation occurs, which resolves within an hour and poses no reason for therapy discontinuation. Sometimes patients report stinging or burning sensation, and itching, however, these sensations also resolve within a couple of minutes. Slight skin tension (when CO₂ penetrates into the tissue) and oedema may occur, however, these also resolve within a few seconds. Some sensitive persons report crackling under the skin.

Undesired effects after the treatment session

Immediately after the treatment patients report the sensation of heat, tingling, and sometimes burning (probably due to the influence of CO₂ on the depolarisation of nerve membranes). Such sensations usually resolve very soon, and the prolonged heat sensation due to vasodilatation resolves within 10 to 20 minutes. Only in sensitive persons the given sensations persist up to 24 hours after the treatment session. If a vessel is hit accidentally, minor hematoma may develop. Ecchymosis, a subcutaneous spot of bleeding, is reported in 5% cases. Exceptionally, in case of administration in the periorbital area, oedema may persist for more than 48 hours.

Planning the frequency and number of treatment sessions

There are basic rules and recommendations related to the number and frequency of treatment sessions, but every patient needs an individual approach depending on the treated locality and their requirements, usually 5-20 treatment, sometimes more.

Durability of results obtained with carboxytherapy

The results will last depending on the lifestyle of the patient. In patients with a healthy lifestyle who drink enough water, refrain from smoking and only drink moderate amounts of alcohol, eat healthy and exercise the results will last for several months to years. On the average, after 5 to 6 months without maintenance therapy it is possible to observe the skin returning to its original condition.

In aesthetic dermatology the vasodilatation effect is taken advantage of together with the effect on the intradermal collagen reorganisation. This effect is observed quite early (usually after two sessions, for example in the course of 7-14 days), as the tonus of the skin as well as its aesthetic parameters improve visibly. Carbon dioxide is used to treat double chin, neck, décolleté, and the lax skin on the abdomen, arms (even after brachioplasty), and the inner thighs as part of body contouring, as well as in post liposuction conditions, to treat lipomatosis, stretch marks, and the skin on the glabella, crow's feet, fine wrinkles around the eyes and the

lower lids – however, here the application of requires a lot of experience. The physician is obliged (in order to achieve a good final result with a combination of techniques) to know the mechanism of action of each treatment modality and optimise the timing of the selected combination. Moreover, it is necessary to inform the patient of the necessity of adequate home care. Combining carboxytherapy with the following treatment modalities is possible on the same day: Before the treatment session it is possible to perform mild microdermabrasion, hydroabrasion, and after the procedure it is advisable to apply a PRP mask or perform a soft laser treatment. After a certain time (in 2 to 10 days according to area to be treated with carboxytherapy) it is possible to perform chemical peels, injection lipolysis, mesotherapy, micro-needling, cell stimulation, cryotherapy, or apply fillers, botulinum toxin, PRP, or Aptos threads, and what needs to be mentioned is that combining carboxytherapy and fillers or PRP also seems very promising [11,13,16,21,24-26,29,34].

For a dermatologist carboxytherapy is a therapeutic modality to be used in patients with poor healing leg ulcers, in patients with peripheral diabetic complications, in therapy of hypertrophic and keloid scars, ill healing surgical wounds, Raynaud's disease, Morbus Burger, acrocyanosis, lymphedema, healing of the skin after the application of skin implants. Carboxytherapy is also effective in the therapy of some symptoms of flexural psoriasis (small psoriatic foci, especially in combination with traditional methods), in circumscript sclerodermia, or in alopecia difusa and alopecia areata, granuloma anulare, necrobiosis lipoidica lichen ruberhypertrophicus forms papules and plaques and is equally difficult to treat (usually with topical corticoids, intralesional corticoids, UVA therapy, antihistaminic drugs, and systemic therapy) [4,12,13,15,16,20,23-27,29,31-34].

Administration of carboxytherapy in other branches of medicine

- **Locomotive organs:** Insufflations of medicinal CO₂ has shown good effects when used to treat patients with vertebrogenic algic syndrome with CBS and LIS manifestations along pharmacotherapy and other methods used in causal therapy” In the administration site insufflations cause analgesia and spasmolysis [7,14,16,18,19,23,30,34].
- **Treat the small joints of the hand:** This treatment is suitable in patients with rheumatic pain or deformities (Heberden's nodes), and in patients after traumas, since the treatment is not painful for the patient but rather effective [19,30-34].
- **Dupuytren's contracture:** There is no clinical experience in a greater number of patients (in our clinic 8 patients), and the recommended treatment is more of a

preventive nature to reduce pain after surgery. The palms of the hands are very sensitive to pain, and it is advisable to apply cooling or anaesthetic gel before administration. Carboxytherapy has successfully been used to support healing after the administration skin implants, and after carpal tunnel surgery [19,30,34].

Carboxytherapy in neurology

According to literature, CO₂ is administered in neurology to manage conditions after encephalitis, Parkinson's disease, vegetative dystonia, or polyneuropathy, whereby very good effects are achieved in migraine and post herpetic neuralgia [11,30-34].

Urology, andrology (Treatment of erectile dysfunction)

Erectile dysfunction, just like other disorders affecting male reproductive organs, (Peyronie's disease, induratio penis plastica) is a serious problem usually managed with medication. Carboxytherapy is an additional treatment modality in the therapy of erectile dysfunction, often with a surprisingly good effect. The aim is to improve blood circulation in the pelvic region, improving erection by reflex action (analogous to shockwave therapy). Carboxytherapy is a secondary method to be combined with other therapeutic methods [20,30,34].

Gynaecology

Decreased blood supply to the genital area, secondary atherosclerosis, and decreased pelvic blood flow through the ilio-hypogastric-pudendal arterial bed, are factors that play a role in the development of vaginal insufficiency syndrome, anorgasmia and female sexual dysfunction. Aesthetic female genital surgery performed to correct the appearance of female genitalia is now becoming increasingly popular at several clinics. Virginal rejuvenation using carboxytherapy has caught the attention of many experts especially due to the fact that it is non-invasive. The administration of CO₂ gas improves blood supply to the pelvic floor and normalises vaginal flora, minimises dryness of vaginal mucosa, revitalises the colour of the vulva, positively influences sexual ageing, and helps manage urinary incontinence. The administration of CO₂ gas in gynaecology and balneology has been recommended as secondary therapy to support the treatment of amenorrhea or oligomenorrhea [11,30,33,34].

Other uses of carboxytherapy

There is no doubt that the utilisation of various types of CO₂ administration is and will be at the centre of interest of many renowned clinics and research teams - for example the utilisation of carboxytherapy in sports medicine could be described in a separate publication.

Conclusion

The advantages of carboxytherapy: in adequate indications, this method seems to be absolutely versatile, safe, physiological, selective, and minimum invasive, covering a very broad therapeutic range. The method is not money consuming, and thus very affordable for the patient, however, the disadvantage is the necessity to repeat the application.

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