CARBOXYTHERAPY
CARBON DIOXIDE INJECTIONS IN AESTHETIC MEDICINE

Carboxytherapy is not a new treatment modality, but has often been under-used in aesthetic medicine. In this article Sabine Zenker provides and overview of treatment protocol for a range of conditions

ABSTRACT
Carbon dioxide therapy is an area of aesthetic practice that has been relatively under-researched, yet widely used. However, those studies that have examined this technique have demonstrated that it improves skin elasticity, circulation and the appearance of fine lines and wrinkles, aids collagen repair, and destroys localised fatty deposits. It is a simple and cost-effective technique. This article reviews the literature available with regard to carboxytherapy and outlines the techniques of treatment.

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KEYWORDS
carbon dioxide injections, collagen, lipolysis, dermal regeneration

CARBON DIOXIDE THERAPY (CDT), or carboxytherapy, is not a new technique within medical practice. Developed in France during the 1930s, it was found that bathing in pools of carbon dioxide-rich water helped to speed up wound healing. By the 1950s, the technique was used by cardiologists to treat patients with peripheral arterial occlusive disease, as well as other conditions caused by poor blood circulation and fat accumulation in the arteries. Since 1995, when the term 'carboxytherapy' was coined, it has increased in popularity in the field of aesthetics, and particularly for lipolysis[1, 2] and dermal rejuvenation treatments. Indeed, studies have demonstrated that CDT improves skin elasticity, circulation and the appearance of fine lines and wrinkles, aids collagen repair, and destroys localised fatty deposits.

Essentially, carboxytherapy is the transcutaneous administration of carbon dioxide for therapeutic purposes. The technique for aesthetic purposes uses intradermal or subcutaneous injections using a medical grade 30 G or 32 G needle to inject sterile carbon dioxide gas, which is delivered using standard programmable apparatus, for the treatment of aged skin, dark undereye circles, localised fat pads, and stretchmarks, for example.

> "The use of carbon dioxide in medicine is not a novel technique, but has been used in medical therapeutics for centuries."

Carbon dioxide: mode of action

Carbon dioxide is an odourless and colourless gas, which, when injected subcutaneously, diffuses at the cutaneous microcirculatory level. As a result, the body will attempt to correct what it considers an imbalance of oxygen/carbon dioxide levels, increasing blood flow to supply oxygen and nutrients to the skin and vessels. This ultimately improves the appearance of the skin. As detailed, however, the use of carbon dioxide in medicine is not a novel technique, but has been used in medical therapeutics for centuries. Reports suggest that in the 17th and 18th centuries it was used to treat chronic skin ulcers ▷

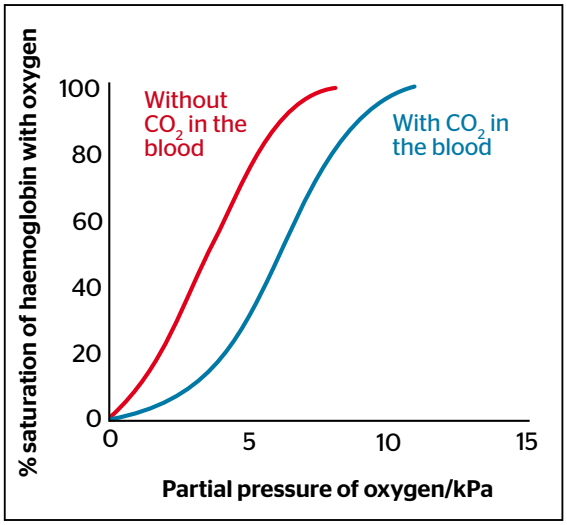

Figure 1 The Bohr's effect. Oxygen levels in the tissue increase oxygenisation (adapted from Albergati et al[7])

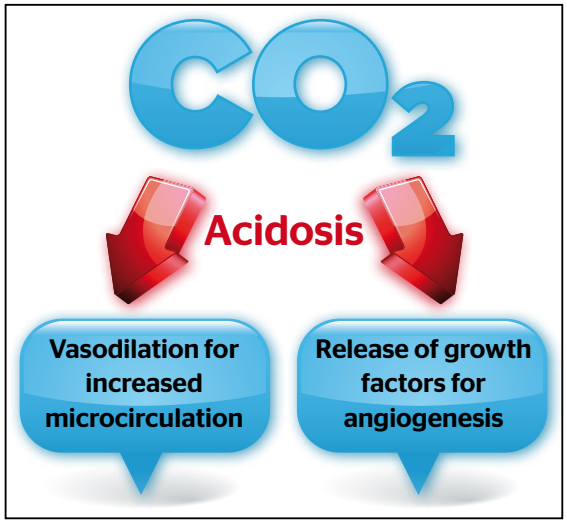

Figure 2 The effects of carbon dioxide (NB. there are far more modes of action than those mentioned here)

▷ and for its anti-infective properties, and interest was reignited during the 1930s to treat organic and functional arteriopathies[4]. The term 'carboxytherapy' to describe the treatment was introduced over 60 years later, in 1995, by Luigi Parassoni during the XVI National Meeting of Esthetical Medicine in Rome[5]. These days, the use of carboxytherapy, particularly in aesthetic and anti-ageing medicine, is now a lot more prevalent and increasing in popularity, particularly throughout Europe. A range of different devices are available with which to administer treatment, but essentially the physician will need a device which meets CE and ISO standards, and has filters to avoid contamination, allows for flow regulation, has a pressure regulator, and administers heated gas in order to reduce pain.

In carboxytherapy, carbon dioxide is introduced to the patient's skin. An excess of carbon dioxide in the injected tissue (hypercapnia) provides the stimulus in the oxygen requirement hypothesis[6]. Approximately 70% of carbon dioxide in the body reacts with plasmatic water to form carbonic acid:

$$CO_2 + H_2O = H_2CO_3$$

And ultimately reacting to leave bicarbonate dissolved in the blood plasma:

$$H^+ + HCO_3^-$$

These reactions cause the pH of the blood to decrease and a release of oxygen to bodily tissue, increasing capillary blood flow. This, in turn, promotes Bohr's effect (the oxyhaemoglobin dissociation curve) (*Figure 1*), which explains how readily haemoglobin acquires and releases oxygen molecules into the fluid that surrounds it. An increased concentration in carbon dioxide leads to a lower binding affinity of oxygen and haemoglobin[7].

Furthermore, the release of growth factors takes places, such as local angiogenic growth factors (*Figure 2*), which induce circulation, encourage lipolysis, and encourage dermal regeneration, for example.

Increased circulation

The overriding point to consider pertaining to increased circulation in carboxytherapy is that hypercapnia improves tissue oxygenation[8]. When applied topically (e.g. as CO_2 water bathing), the increase in carbon dioxide concentration within the tissue and peripheral blood vessels causes precapillary arterioles to dilate, ultimately increasing blood flow to the skin[9]. Hypercapnia further lowers the resistance of the arteries in the skin and muscles, which dilate on account of the decline in pH. This takes place even with carbon dioxide administration into the skin[10]. Curri and Bombardelli[11] reported the verification of this increased vasodilation in the arterioles and metarterioles, as well as the increased vasomotion, using optic video capillaroscopy. The ▷

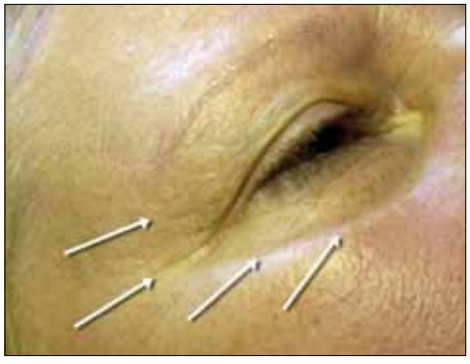

Figure 3 Technique when treating the periorbital area—typical injection points

Figure 4 Skin appearance during and after treatment of the periorbital area: (A) within 2 minutes; (B) 4 minutes; and (c) 6 minutes

▷ evidence, therefore, shows that carboxytherapy acts on the microcirculation at the level of the metarterioles, arterioles and precapillary sphincters, by increasing tissue flow velocity and improving lymphatic drainage as a result.

One area in which carboxytherapy is used for circulation is in water bathing for arteriopathy, providing vasodilation and neovasodilation at the microvascular level[12]. One study showed that vasodilation is mediated by nitric oxide, which induces neoangiogenesis *in vitro*[13], while another showed that collateral blood flow in ischaemic hindlimb was enhanced via the mobilisation of endothelial progenitor cells[12]. When using transdermal carbon dioxide application to treat diabetic foot ulcers, Wollina et al found an improvement in granulation and a reduction in discharge after 1 week of treatment[14]. However, the authors did note that further prospective trials were necessary. In another study[1], which examined the use of intradermal and subcutaneous carboxytherapy for the treatment of localised fat pads and cellulitis, the authors noted two significant microcirculatory changes after the administration of the therapy: an increased perfusion as measured using laser Doppler flowmetry, and an increase in oxygen tension (Bohr effect on the oxygen dissociation curve).

Lipolysis

Brandi et al[1] showed that carboxytherapy positively affects the physiological oxidative lipolytic process:

'The data regarding measurements of the maximum circumference of the thigh, knee and abdomen taken before and at the end of the treatment showed a significant reduction in all patients.'

Again, the treatment was found to be highly effective when administered subcutaneously for localised fat pads/cellulitis. During such treatment, it has been noted that the adipose tissue fractures, lysis of adipocytes occurs, and triglycerides are released into the intracellular spaces; none of the vascular structures are adversely affected during this treatment. A similar study found a significant reduction in the mean ▷

“The data regarding measurements of the maximum circumference of the thigh, knee and abdomen taken before and at the end of the treatment showed a significant reduction in all patients.”

Figure 5 Under-eye puffiness. (A) Before treatment and (B) 2 months after the first treatment (four treatments were performed in total). (C) Before treatment and (D) 3 months after three treatments. (E) Before treatment and (F) 1 month after four treatments

Figure 6 Subcutaneous injections to the submental area

Figure 7 Treatment of localised fat pads – before (A) and after (B) three treatment sessions (using RioBlush)

▷ upper, mid and lower abdomen circumference in three different age groups who had been treated with carbon dioxide therapy, as well as significant weight loss and a reduced thigh circumference[15]. No serious complications were reported, and the author concluded that carboxytherapy is both safe and effective. These results align with those originally reported by Brandi[1], and demonstrate that this treatment modality is both safe and effective. Carboxytherapy has also shown to be effective when administered postoperatively, after liposuction for example. Jose Leon-Solarte, in a presentation at the 2007 American Academy of Cosmetic Surgery, detailed that out of a total of 40 patients treated over a 6-week period, 34 (85%) had a dramatic improvement in cutaneous flaccidity, and the remainder (15%) had partial results.

Dermal regeneration

Intradermal carboxytherapy for the treatment of ageing or damaged skin was developed from an animal-based blind, interventional, cross-sectional study, which injected carbon dioxide into the dermis of wistar rats[3]. The control group received injections of saline. The researchers in the study observed the compacting of collagen fibres following the infiltration of carbon dioxide, and especially when this took place intradermally. Furthermore, there was a notably improved appearance in the skin, as well as intense collagen turnover. The use of CDT on damaged or ageing skin also results in a thicker appearance of the dermis, the collagen fibres being distributed more diffusely[1], and stimulates collagen synthesis[3]. This means that carboxytherapy can also be used to improve scar tissue through the increase in collagen deposition and reorganisation, and the improvement in skin texture and tone[16].

Carboxytherapy for aesthetics

It is not surprising therefore, that carboxytherapy is now used as an aesthetic treatment to improve skin laxity and the overall appearance. The therapy can be used to treat ageing skin on the face and décolletage, dark undereye circles, stretch marks, cellulite, and localised fat pads. However, as with any medical treatment, there

Figure 8 Clinical results of skin rejuvenation, before (A) and after (B) 10 treatment sessions

are contraindications that the physician should take into account:

- Acute, untreated cardiovascular disease, uncontrolled blood pressure, and vasovagal episodes
- Acute respiratory problems
- Bleeding syndromes, cerebrovascular accident (stroke), acute thrombosis or recent pulmonary embolism
- Connective tissue disease
- Skin infection
- Uncontrolled diabetes
- Pregnancy and lactation (although no data is available in this regard).

It is also important to note that with carboxytherapy there is an absence of toxicity and any other relevant side-effects.

Injection techniques and treatment protocols

Depending on the type of treatment to be performed, the injection technique will vary. Intradermal injections should be used for dermal rejuvenation, while subcutaneous injections are reserved for lipolytic effects. When injecting for skin rejuvenation, the injection is performed intradermally using a 30G needle. The injection angle should be maintained at <15º with bevel border up. Immediately after injection, the CO_2 gas diffuses into the needle-surrounding tissue. The clinical endpoint of each injection is at the occurrence of an erythema and distension of the injected tissue. The flow of the CO_2 gas has to be adjusted individually. For subcutaneous injections, the injection will be into the subcutaneous structures; the injection angle should be 30–45º, using a 30G needle. The same clinical endpoints will determine each injection. The gas should be cold for fat pad treatment, as it seems to be more effective (although the author was unable to find any evidence in the literature to support this).

> **“Carbon dioxide therapy can be used to rejuvenate the skin on the face, décolletage, neck and hands, and improves rhytides, withered skin, fine wrinkling, lost tissue luminosity and skin laxity.”**

Periorbital area

When used in the periorbital area, carboxytherapy can treat rhytides, dark circles, vascular pooling, tissue luminosity, skin laxity, and mild fatty prolapse. Dark circles and wrinkles should be treated with intradermal injections, while mild fat pads should have a mix of intradermal and subcutaneous injections. Flow should be up to 40–60cc/min, with warm gas and using a 30G needle. Generally, patients will receive four to eight sessions, with one session every 2–4 weeks. The technique and typical injection points are shown in *Figure 3*. Injections are usually painless, so anaesthesia is rarely used, but the patient will feel a warm sensation on injection (vasodilation). Between 5 and 10 minutes following injection, an erythema will occur around the treated area and the upper eyelid will inflate (*Figures 4* and *5*). However, no post-treatment care is necessary, and the appearance of the eyes after the prescribed number of sessions is greatly improved (*Figure 5*).

Facial fat pads

To treat mild under-eye fatpads, a mixture of subcutaneous and intradermal injections should be used. Subcutaneous injections alone should be used for mental fat pads. Indications for the use of carboxytherapy in the submental area include skin laxity, prejowl sulcus, an undefined jawline, and a mild fat pad under the chin. Techniques and results are shown in *Figures 6–8*.

Dermal rejuvenation

Carboxytherapy can be used to rejuvenate the skin on the face, décolletage, neck and hands, and improves rhytides, withered skin, fine wrinkling, lost tissue luminosity and skin laxity. Using a 30G needle, flow should be up to 80cc/min, with intradermal injections spaced out by 1–2cm. Patients will generally receive between four and eight treatment sessions every 3–4 weeks. Clinical results are shown in *Figure 9*. ▷

Figure 9 Skin rejuvenation on the neck, before (A) and after (B) eight treatment sessions (using RioBlush)

Figure 10 Clinical results when treating stretch marks on dark/pigmented skin; (A) before treatment and (B) after eight sessions

▷ Stretch marks

When treating stretch marks with carboxytherapy, it is better to perform the technique on old, white depressed marks rather than young, red stretch marks. Also, deep striae are better than thin striae. Contraindications for this treatment protocol are infection, pregnancy and anti-coagulation. Treatment should combine intradermal and subcutaneous injections using warm gas and a 30G needle. The flow should be up to 80–150cc/min. More often than not, the patient will not necessarily experience any pain with this treatment as the stretchmarks already represent ruptured tissue; this means that the gas can diffuse more easily and is therefore less painful. Results are usually seen between four and 10 sessions, and should be maintained with two to three sessions per year. After injection, patients may experience the popcorn effect, erythema and a warm sensation, but clinical results are excellent (*Figure 10*). It is necessary to explain the typical popcorn effect: this shows up only in the treatment of stretchmarks and relates to the fact that the ruptured tissue of the stretchmarks allows the gas diffuse far more easily, with the CO_2 'popping' the skin up. This effect will fade after approximately 10 minutes, although an erythema sometimes remains for a little while longer.

> "Carbon dioxide therapy is a simple and cost-effective technique with minimal side-effects."

Conclusions

Carboxytherapy refers to the cutaneous and subcutaneous administration of carbon dioxide gas for therapeutic purposes. By injecting small amounts of carbon dioxide gas into dermal and subdermal structures (such as fat), the body is triggered to increase the oxygen flow to the area injected, and consecutively increases collagen neogenesis as well as lipolysis. Therefore, the most common indications for CDT are skin flaccidity, sun-damaged skin, dark under-eye circles, localised fat pads, stretch marks, and cellulite. Its ease of use, cost-effectiveness and safety makes CDT a successful treatment in aesthetic medicine. To further prove the efficacy of carboxytherapy, however, further clinical trials are necessary.

▶ ***Declaration of interest*** *None*

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Key points

- Carboxytherapy refers to the cutaneous and subcutaneous administration of carbon dioxide gas for therapeutic purposes
- The most common indications for carboxytherapy are skin flaccidity, sun-damaged skin, dark under-eye circles, localised fat pads, stretch marks, and cellulite
- Studies have demonstrated that carboxytherapy improves skin elasticity, circulation and the appearance of fine lines and wrinkles, aids collagen repair, and destroys localised fatty deposits

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