Carboxytherapy in Aesthetic and Regenerative Dermatology

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11.1 Introduction

Carbon dioxide (CO_2) therapy refers to the transcutaneous administration of CO_2 for therapeutical purposes. Historically, CO_2 therapy started in the year 20 B.C. (discovered in France) and rediscovered in the Middle Ages. Since 1932, this was used scientifically in France at the RoyatSpas for the treatment of patients affected by obliterating arteriopathies (CO_2 was diluted in water and given transcutaneous). The use of CO_2 inside the body is not new; from the year 1914, CO_2 was used in Radiology as a contrast element for kidney studies and in laparoscopic surgery since 1924, because of its incombustible properties. The transdermal technique is still used for arterial disease, chronic wounds, and Raynaud Syndrome with good results [1–5].

In this chapter, intradermal and subcutaneous administration of CO_2 is discussed.

CO_2 administration proved to be effective not only in improving local parameters of circulation and tissue perfusion, but also in inducing a partial increase in transcutaneous PO2. Such might be due to a hypercapnia-induced rise in capillary blood flow, a drop in cutaneous oxygen consumption, or a right shift of the Oxyhemoglobin dissociation curve (Bohr effect) as shown in Fig. 11.1. As such, the effect of carbon dioxide therapy on the microcirculation, and the probability of a positive effect upon the physiological oxidative lipolytic process, led to the use of this gas in the treatment of localized adiposities. Some authors have furthermore demonstrated the coexistence of an increase in subcutaneous localization of fat with alterations in blood and lymphatic drainage [6].

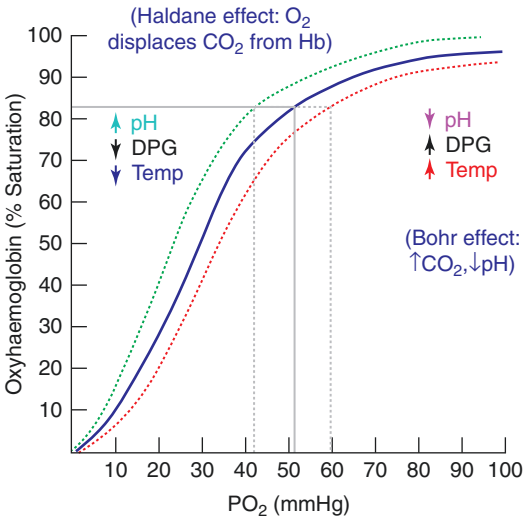

Fig. 11.1 Oxyhemoglobin dissociation curve. Bohr effect

When injected inside or under the skin, CO_2 stimulates vasodilation and neoangiogenesis. The hypercapnia induced-rise in capillary blood flow is produced, accelerating metabolic changes

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and the lipolytic process. Cellular trophism is improved since interstitial CO_2 enhances tissue oxygenation by forcing oxyhemoglobin to liberate O2 (Bohr effect). There is a decrease in fibrosis [6] that can be perceived in successive treatments [1, 7]; this has a stimulating effect on the dermis [4, 8]. Histologically, the injection of CO_2 into subdermal adipose tissue has a lytic effect on adipocytes respecting vascular and nerve structures as demonstrated by Brandi et al. in 2001 and Balik et al. in 2011 [6, 9].

Berthier introduced CO_2 in the treatment of Cellulite in 2000 [10, 11]. Brandi published in 2001 the effects of Carboxytherapy in adipocytic lysis [6], and in 2004 its tensor effect [12]. In 2008, carboxytherapy was found to produce collagen synthesis [4]. There is also the mechanical undermining by the gas flow similarly like in needle subcision (e.g., in the treatment of scars, adhesions, or severe cellulite depressions). There are effects of mechanical tension on the cells (especially in rejuvenation) and pressure (especially in the treatment of cellulite or adiposities) resulting from relatively strong gas flow during the CO_2 administration. Presumably there is also some slight influence of temporary acidosis [13]. When injected intradermal, thickening of the dermis and rearrangement of collagenous fibers is shown to be increasing skin elasticity, as demonstrated with histological studies by Brandi et al. [6] shown in Figs. 11.2 and 11.3. Changes are probably due to improved microcirculation and oxygenation of the tissue [14]. This effect leads to tightening the skin and decreasing flaccidity.

Therefore, intradermal and subcutaneous administration of CO_2 (Carboxytherapy) is being used as a medical non-invasive or minimally invasive treatment for many inaesthetic conditions [10, 11].

Carboxytherapy is a safe procedure and is a good alternative in the removal and treatment of various skin and subdermal defects and inaesthetics [2]. CO_2 is drained into de blood vessels and eliminated by the lungs; while a little portion is converted into carbonic acid and is eliminated through the kidneys [10].

11.2 Treatment

Required material:

- CO_2 pressurized bottle/tube for medical use.
- Pressure regulator.
- Carboxytherapy device.
- Particle filter.
- Connection tubes.
- 30G–31G 13 mm and 4 mm long needles
- Remember what is required for intradermal/subdermal sterile technique: gloves, 95º Alcohol/2% Chlorexidine

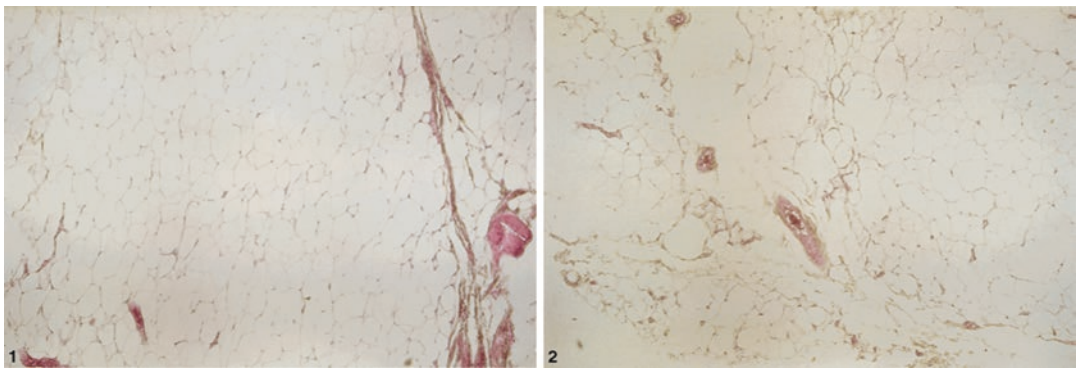

Fig. 11.2 Histology of the subcutaneous adipose tissue (from Brandi et al. [6] with permission). (1) Histological features of the subcutaneous layers before CO_2 treatment. (2) Histological appearance of the subcutaneous layers after CO_2 treatment, showing lysis of the adipocytes not involving the vascular structures

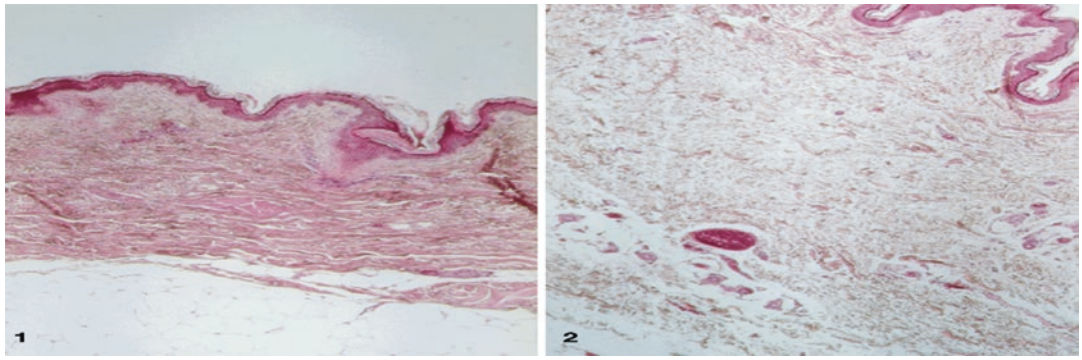

Fig. 11.3 Histological features of the Dermis (from Brandi et al. [6] with permission). (1) Histological appearance of the dermis before CO_2 treatment. (2) After CO_2 treatment, thickening of the dermis and rearrangement of collagenous fibers is shown

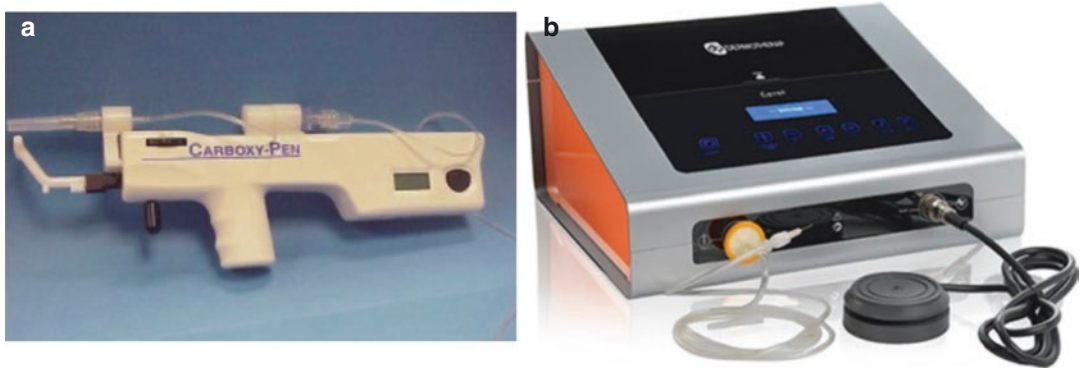

Fig. 11.4 Carboxytherapy Devices. (**a**) Carboxipen is a manual mesotherapy gun for injecting CO_2. (**b**) Coral is an automatic device

There are currently many Carboxytherapy devices available; some of them are manual or gun-like devices for mesotherapy (Fig. 11.4). For aesthetic medicine a very precise tool is required with the ability to apply very different volumes of the gas with different flows depending on the indication, state, and the compliance of the patient. The author prefers automatic devices as shown in Fig. 11.5. The CO_2 flow should be adjusted manually, as well as the gas temperature and the volume. Some devices include preloaded therapeutical programs and there are many brands and worldwide availability. Prices are affordable.

11.3 Technique

First of all, there has to be a full clinical evaluation, diagnosis, a detailed assessment of the skin, and the inaesthetics that has to be treated. As shown in Fig. 11.6, the treating physician has to define the volume to be used according to the pathology and deepness to be treated. Always warm the gas (usually the machine is automatically set to 28 °C). Then choose the right flow, according to the area and patient's personal and local sensitivity. The environmental air of the system should always be purged, so that it con-

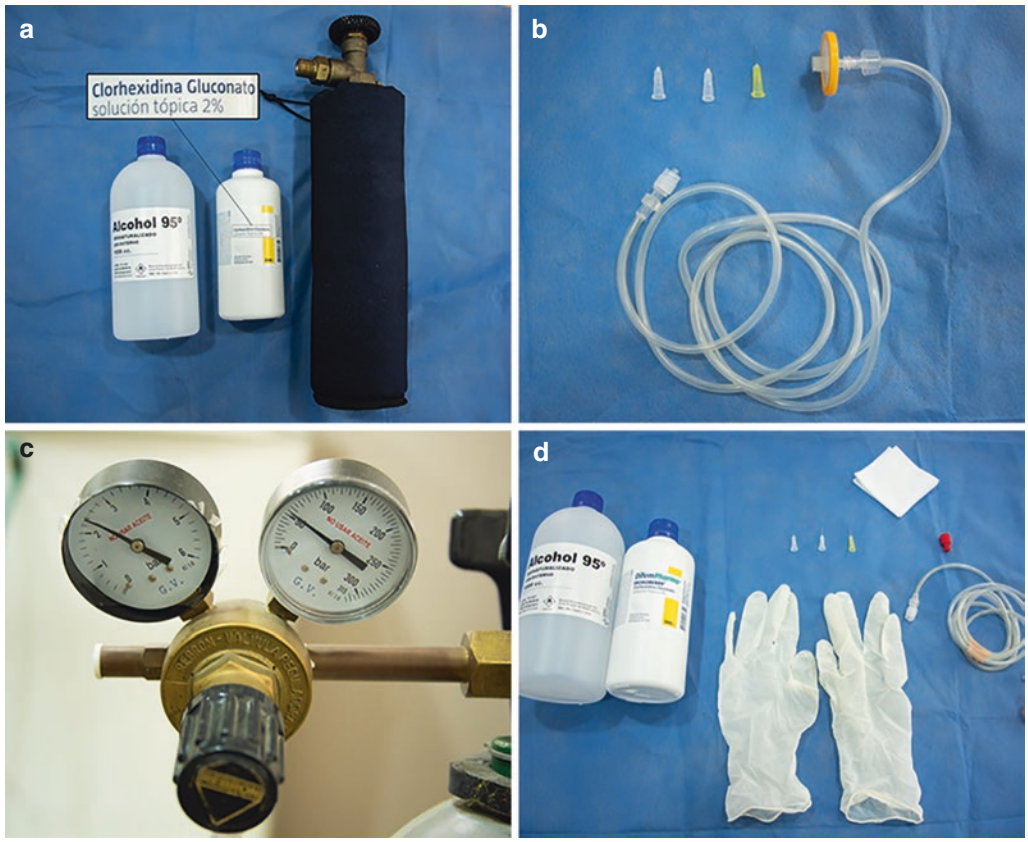

Fig. 11.5 Necessary materials. (**a**) CO_2 pressurized tube. Alcohol and Clorhexidine. (**b**) Particle filter and sterile tube for injection. 30G 1/2-inch (13 mm) needle. 31G 13 mm and 4 mm needles. (**c**) Gas flow regulator. (**d**) Gloves for asceptic technique

tains only CO_2. If the tubing system contains ambiental air, too much inflammation may occur.

Never use local anesthesia, since it is not required and may disturb the skin before the treatment. No topical anesthesia is required, neither electrical nerve stimulation (TENS) [15] or cold pads.

The needle should be introduced with a 45-degree angle into the skin with a sterile technique as shown in Fig. 11.7. For intradermal treatment, the angle should be less. The needle has to be attached through the connecting tube to the Carboxytherapy device. Only then, the treating physician is ready to push the button or pedal and start the injection of the gas.

2000 cc is the maximum dose. Higher than 2 Liters, patient may feel dizzy, because of hypercapnia. Volumes to be used depend on the pathology or inaesthetics.

It is best to do treatments every 2 days depending on the diagnosis. Most patients will get skin improvements after 2–3 weeks of treatment. When treating subdermal fat, best results are obtained in 10 weeks.

11.4 Precautions

Certain precautions should be taken when performing Carboxytherapy treatments.

- It is a medical procedure, minimally invasive and should be performed by a physician.
- Always use skin-approved antiseptics.

Fig. 11.6 Treatment settings. (1) Select mode (preset settings or manual settings). (2) Warm gas: always. (3) Set flow. (4) Select dosage system. (5) Set volume to be injected. (6) Always purge tube system. (7) Device is ready to do treatment

- For sensitive skin (face, periorbital), prefer 2% Chlorhexidine.
- Do not allow massage after the procedure for 8 h.
- Patient can return to normal activities after the procedure.
- Compression stockings or sashes are desirable.

11.5 Advantages

The treatment should be done by a trained physician; not by a non-medical professional. Furthermore, this procedure cannot be performed in a non-medical facility. It is a minimal invasive treatment, completely outpatient with fast sessions (no more than 20 minutes), and small areas can be treated without anesthesia. If done properly, there should be no side effects other than those described below, and they are transient.

One of the greatest advantages is that residual adiposities, such those left after a liposuction, can be treated and the body contour can be regularized.

The periocular area is of concern because of flaccidity, wrinkles, and dark circles. Carboxytherapy is a very good tool to treat these inaesthetics.

On the other hand, carboxytherapy devices are inexpensive and require little maintenance. CO_2 is also an inexpensive gas.

11.6 Disadvantages

Carboxytherapy treatments have 3 disadvantages. First of all, many sessions are required. Some patients may feel impatient. It is important to set real expectations on the clinical results of this minimal invasive treatment. Treating patients with very high expectations is not recommended.

Few patients dislike some of the side effects, even though they are mild, transient, and well tolerated by the great majority of patients.

Most of the devices do not require maintenance, but for some automatic devices technical support available is needed.

11.7 Side Effects

Side effects are mild, transient, and well tolerated by the vast majority of patients.

- Crackling sensation in the area of injection that lasts for 1–2 h.
- Pain at the site of injection (about 75% of the patients); it is handled by heating the gas up to 28 °C and decreasing the flow.
- Hematomas at the site of injection that may last up to 4 days and are not of aesthetic concern.

There are some clinical conditions where carboxytherapy is contraindicated as shown in Table 11.1.

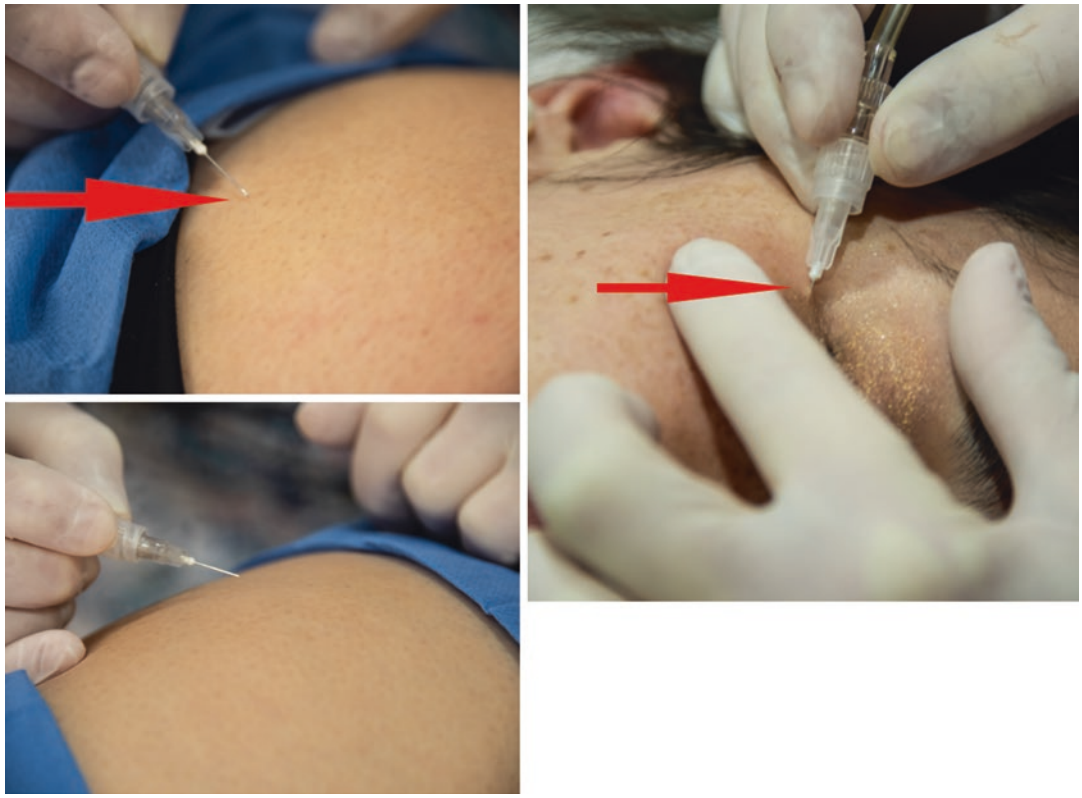

Fig. 11.7 Needle insertion techniques. For subdermal treatment, a 45° angle is best. For intradermal treatment an acute angle is required. Note that in the periocular area the tip of the needle can be seen beneath the epidermis

Table 11.1 Contraindications

• Severe respiratory insufficiency
• Severe renal failure
• Chronic congestive heart failure
• Patients treated by carboanhydrase inhibitors (e.g., acetazolamide, diclophenamide)
• Severe anemia
• Chronic liver insufficiency with decrease of plasmatic protein levels
• Gaseous gangrene (Clostridial infection)
• Pregnancy
• (Breastfeeding)
• Infection on the site of treatment
• Psychiatric disorders

11.8 Complications

Complications are rare. Some infectious complications may be possible; there is a Mycobacterium atypical infection after mesotherapy described by Herreros in 2008 [16]. Also, massive subcutaneous emphysema after carbon dioxide mesotherapy is described by Calonge et al. in 2012 [17]. There is no history about who and where the procedures were done. If 2000 ml in one session are exceeded, dizziness may appear. It is transient and just requires 30 minutes rest.

Avoiding complications is mandatory for any aesthetic treatment. The procedure has to be performed by a trained medical physician in a medical procedure ward [18].

11.9 Aesthetic Indications of Carboxytherapy

1. Skin Rejuvenation. Flaccidity (facial, neckline, or corporal).
2. Periorbital area: wrinkles or dark circles.
3. Cellulite.
4. Localized adiposities.
5. Stretch marks.

6. Chronic wounds.
7. Skin grafts.

11.9.1 Flaccidity; Skin Rejuvenation

Because of its effect on dermal collagen, CO_2 may be used in any area of the body [11, 19, 20]. With multiple punctures and low CO_2 doses separated by a few centimeters [10]. With a 31G needle and doing a little emphysema with 5–15 cc CO_2 at every puncture. Better to use lower gas flow (50–70 ml/minute) and intervals of 15 days for each session. Skin of the face, neckline, or corporal can benefit from this treatment as shown in Figs. 11.8 and 11.9.

11.9.2 Periorbital Area

In this area the greatest inaesthetics are wrinkles and flaccidity [8, 18, 21, 22]. With a 31G needle with the bezel facing up, the emphysema will be very visible as shown in Fig. 11.10. It is not necessary to use more than 80–100 cc in each periorbital area. Low flow of CO_2 is better for this area (50 ml/minute). The emphysema will be visible for hours; and in very sensitive skin, erythema might last 2 days.

Dark circles are of concern in this area, too. This can be of congenital cause (ethnic), but the most cases are from iron deposits due to chronic periorbital inflammation. Because of the vasodilation and increased capillary flow that occurs due to local hypercapnia, these dark circles can be treated. The mechanical effect produced by the gas flow puts pressure on the iron deposits and pushes them into the dilated capillaries. Usually good results can be achieved in 3 weeks of treatment.

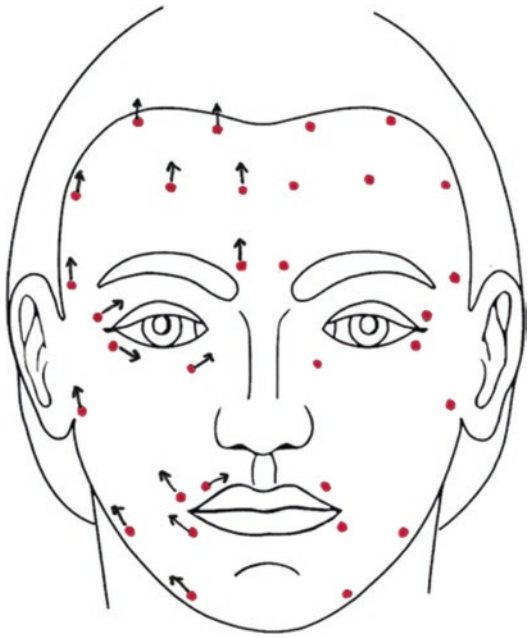

Fig. 11.8 Scheme of application of Carboxytherapy for facial rejuvenation—modification after J.C. Lopez (Sao Paulo, Brazil). It is not necessary to inject in all these points and it depends on the state of the skin, observed gas spreading, and compliance of the patient

11.9.3 Cellulite and Gynoid Lipodystrophy

Cellulite is an irregular alteration of the skin surface giving orange or cottage cheese appearance. It happens in 90% of women, independent of ethnicity. In advanced stages can be painful. Histologically there is fibrosis, lymphedema, and fat globules found in the subdermal tissue. This condition worsens with aging, because flaccidity of the skin and subdermal tissue [8, 23, 24].

Carboxytherapy is used among other treatments, because of its unique effect on the subdermal adipose layer [23, 25, 26]. Its infusion into the affected site produces mesolipolysis and aims to remove cellulite and improve skin texture [27, 28].

- Improves blood and lymphatic flows, which facilitates drainage of the retained liquid.
- Improves the tone of the skin, which restores elasticity and counters the typical sagging in Gynoid Lipodystrophy (GLD).
- Reduces fatty deposits and, consequently, the orange appearance of the skin.
- Fights fibrosis because it improves blood microcirculation and restores skin elasticity

Fig. 11.9 Face treatment. 31G 4 mm needle is used. Note the deepness of the dermal injection. Use 10 to 15 ml in each puncture. Little emphysema can be seen after every puncture

(decrease of the characteristic dimples of the skin with cellulite).

Carboxytherapy is effective to treat buttocks, thighs, abdomen, and local adiposities of the knees [10, 26, 27] as shown in Fig. 11.11. The volume to be injected is higher than other treatments; 800–1000 ml each side. Gas flow may be high: 100–120 ml/minute, depending on patient tolerance.

11.9.4 Localized Adiposities

Local adiposities may be inaesthetics in any part of the body (Fig. 11.12). It affects young and old patients; and residual adiposities may remain after a liposuction surgical procedure [12]. Carboxytherapy is an excellent tool for body contouring.

Carboxytherapy produces a lipoclastic effect on fat tissue, as demonstrated by Brandi [6] and Balik [9] without effects on the blood vessels or nerves and it is a secure procedure [29]. A 30G needle is best for this treatment, since higher flow can be used in this area (up to 200 cc/min) and higher volumes are required as well; depending on the size of the adiposity 200–1000 cc. Remember to never use more than 2 Liters in one session, since the patient may get dizzy due to transient hypercapnia.

Fig. 11.10 Carboxytherapy for Periocular area. Note the deepness of the needle entrance into the dermis. The emphysema is seen in both eyelids. 50 ml were used each side. (**a**) Carboxytherapy for under eye circles © Jindal P. et al.; 2020 (with permission)

11.9.5 Stretch Marks

Stretch marks (striae distensiae) are fractures of collagen fibers within the dermis (dermal scars). Brandi et al. [6] showed thickening and an increase and rearrangement of collagen fibers in the dermis after CO_2 treatment [4, 12] and Hodeib showed an increase of fibronectin in stretch marks [30].

Better results are obtained in recent start of this condition, when stretch marks are red or pink. In more advanced stages they become pale and atrophic; better results in advanced stages are obtained with laser (resurfacing with ablative fraxel laser).

Fig. 11.11 Cellulite. Treatment of a thigh with local adipocity in the medial aspect of the knee. Note the angle of needle insertion, emphysema (200 ml), and skin erythema

Fig. 11.12 Injection of CO_2 into a local adiposity on the flank. Note the angle of insertion of the 30G needle, the emphysema and erythema obtained with 200 ml CO_2 in the subdermal fat

Treatment should be done in each stretch mark and to its full extent. 30G or 31G needles are well tolerated using the intradermal technique. Including a low flow of 50–70 ml/min and enough volume for filling each stretch mark found in the treated area as shown in Fig. 11.13.

11.9.6 Chronic Wounds

A wound is defined as chronic when it does not heal according to the normal repair times and mechanisms (Fig. 11.14). This particular condition may be principally due to local hypoxia. Carboxytherapy refers to the transcutaneous or subcutaneous administration of CO_2 for therapeutical effects on both microcirculation and tissue oxygenation [18, 31].

Carboxytherapy administered subcutaneously may be used in addition to the routine methods of treatment for such lesions (surgical and/or chemical debridement, advanced dressings, compression, etc., according to the features of each lesion). Brandi et al. found significant improvement in progress of the lesions in terms of both healing and reduction of the injured area with Carboxytherapy [31].

For chronic wounds the same technique as for grafts is suggested.

Fig. 11.13 Stretch marks treatment. Note the angle of needle punction. Each stretch mark should be punctured and filled with gas. Emphysema should appear in everyone and erythema in the whole area

11.9.7 Skin Grafts

Skin flaps and grafts procedures are widely used to reconstruct skin and soft tissue defects. Skin flap necrosis is a serious postoperative complication. Many groups work with transcutaneous CO_2 [32]. Carboxytherapy increases blood flow and tissue oxygenation [7, 15]. Nisi and Brandi concluded in their study that CO_2 injection enhances the inflammatory response of the implanted tissue and reduces the reabsorption rate. The treatment may improve the graft survival [3].

For intradermal and subdermal injections of CO_2, same technique as for flaccidity; many applications with 31G needle and low volume (10–20 cc) with low flow (50 ml/min) in the healthy tissue surrounding the graft or flap.

11.9.8 New/Other Indications

There are some other new indications for Carboxytherapy, such as different type of scars (acne, surgical), erectile dysfunction associated with microangiopathy, treatment of hair disorders; sometimes it helps to improve psoriasis, scleroderma and, paradoxically even angiectatic rosacea. In short, any skin conditions that require vasodilation [10].

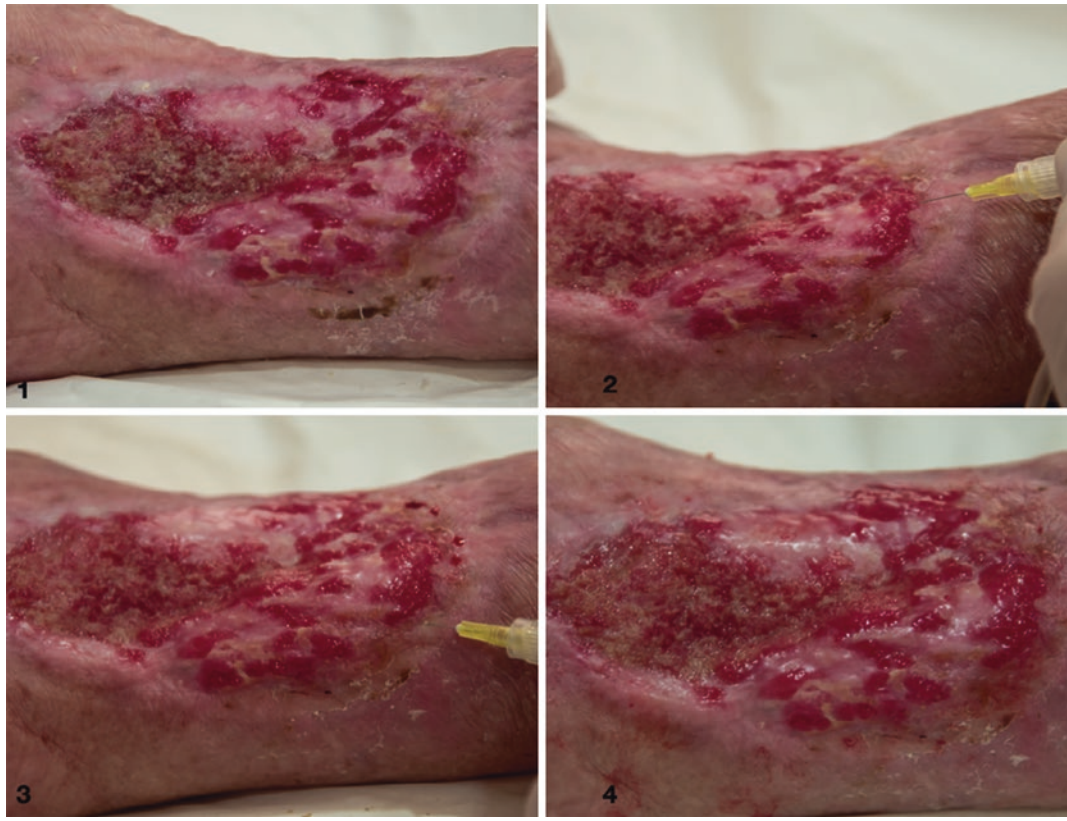

Fig. 11.14 Carboxytherapy in Venous Leg Ulcer. (1) Previous to treatment. Severe lipodermatosclerosis is seen. (2) Note the angle of the puncture using a 30 G ½ inch needle. (3) 5–10 ml in each puncture. Little emphysema is noticed from hardening of the skin. (4) Note erythema and emphysema after treatment

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