Effect of Carbon Dioxide Facial Therapy on Skin Oxygenation

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ABSTRACT

Background: Recently popularized in the field of cosmetic dermatology, subcutaneous carbon dioxide (CO2) injections have been shown to improve the skin's appearance by augmenting oxygen delivery and thereby aiding cellular metabolism and neocollagenesis. However, they carry several risks and cannot be used on the entire face, leaving them best suited for the treatment of localized skin concerns. To combat these issues, a less invasive CO2 facial suited for full-face treatment has been developed, though its efficacy in oxygenating the skin has not been thoroughly investigated.
Objective: The aim of this study was to evaluate the ability of the CO2 facial to oxygenate the skin.
Methods and Materials: Twelve patients were enrolled in this split-face study. They were treated one week apart with a CO2 facial on one side of the face and particle-free microdermabrasion on the other. Measurements of transcutaneous oxygen tension (tcPO2) were recorded at baseline and after each treatment. Statistical significance was assessed by comparing the average tcPO2 difference in mmHg following microdermabrasion and after a carbon dioxide facial using a 1-tailed paired t-test ($\alpha = 0.05$).
Results: The average increase in tcPO2 after CO2 facial treatment was statistically significantly greater ($p = .0252$) than after microdermabrasion.
Conclusion: Carbon dioxide facials improve skin oxygenation immediately following treatment, attributable to the generation of an artificial Bohr effect.

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INTRODUCTION

Well known as a substrate in various metabolic and energy-dependent processes, oxygen (O2) is necessary for repair and regeneration of the skin.[1,2] Consequently, in a society that increasingly equates youth with beauty, the role of O2 in skin care has received considerable attention. Oxygen-themed products and recently popularized oxygen facials claim to improve elasticity, diminish the appearance of fine lines and illuminate the skin. However, the stability of oxygenating compounds in topical products is questionable and their ability to penetrate the stratum corneum, as well as their general efficacy, has not been clinically proven.

Subcutaneous carbon dioxide (CO2) injections have become increasingly popular in the field of aesthetic medicine given their ability to promote oxygenation of the skin from the underlying microcirculation.[3] Unlike the topical application of oxygenating compounds, this technique ensures unimpeded delivery of O2 to tissues by generating a Bohr effect that exchanges O2 with CO2 at the level of dermal capillaries. Microcirculatory changes owing to the transient delivery of CO2 improve skin perfusion and facilitate nutrient delivery and waste disposal.[4]The ensuing supply of oxygen stimulates collagen production and accelerates cellular metabolism.[3,5,6,7] For this reason, subcutaneous CO2 injections are often used to promote dermal regeneration and thereby reduce the appearance of fine lines, scars and hyperpigmentation.[4,8]

A novel facial treatment recently emerged that combines the science of carbon dioxide therapy with mechanical exfoliation. Unlike subcutaneous CO2 injections, the CO2 facial generates CO2 bubbles on the skin surface, which permeate the epidermis with minimal discomfort. To assess its ability to oxygenate the skin beyond what is expected following mechanical exfoliation, and thereby assess its ability to produce the Bohr effect, we performed a split-face study that compared changes in transcutaneous O2 tension (tcPO2) after CO2 facial treatment with those following a standard microdermabrasion procedure.

METHODS

This was a single-center clinical trial performed on 12 self-selected healthy male and female patients ranging in age from 23 to 64. Patients gave informed consent of the format utilized by the Western Institutional Review board, which conforms to the ethical guidelines set forth in the 1975 Declaration of Helsinki. Standard Operating Procedures for Clinical Research in accordance with the appropriate Moy-Fincher-Chipps oversight committee and Good Clinical Practice was observed.

The inclusion criteria were healthy, self-selected male and female patients of any racial/ethnic origin and any Fitzpatrick skin type aged 20-65 years old. Exclusion criteria included current or history of skin cancer, pregnancy, lactation, active dermatologic conditions in the treatment area, vascular disorders in the treatment area, recent use of resurfacing products or treatments on the treatment area, known allergies to cosmetics or other products, any surgical, invasive, or ablative procedure in the treatment area within three months prior to treatment or before complete healing, face lift, eyelid surgery, skin resurfacing, deep chemical peeling or deep dermabrasion in the treatment area within three months prior to treatment or before complete healing, injected chemical substance, threads, or synthetic fillers in the treated area within two-three weeks prior to treatment or before complete healing has occurred, botox in the treated area within 2 weeks prior to treatment or before complete healing has occurred, and severe active acne.

At the start of the trial, each subject was randomly assigned the carbon dioxide facial or microdermabrasion procedure as his or her first treatment. Determination of what side of the face would be treated was also randomized. In order to minimize crossover between treatments and account for individual variations in skin perfusion and oxygenation, the remaining procedure was performed a full week later on the same patient and on the opposite side of the face.

The carbon dioxide facial that was the focus of evaluation in this trial is an aesthetic device by the name of OxyGeneo™ (Dermaspark Products Inc, Vancouver, British Columbia; Pollogen Ltd, Tel Aviv, Israel). For comparison of tcPO2 following standard microdermabrasion, the Dermasweep MD Multi-Level Skin Resurfacing System (CosMedic R&D Inc, Roseville, CA) was used. The carbon dioxide facial was performed using a handheld applicator and capsule along with one of two nutrient gels chosen by the patient in accordance with their skin care needs (Figure 1). Particle-free microdermabrasion was performed in three passes on dry skin using a microdermabrasion wand hand piece and medium level treatment tips (.006 Level Polyester).

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The same measurement protocol was followed for each treatment. The cheek of each subject was wiped clean with alcohol on the pre-assigned side of the face. An electrode was placed and then connected to a tcPO2/TCOM monitor (PeriFlux system 5000, PeriMed Instruments). To allow adequate time for equilibration, a baseline transcutaneous oxygen tension (tcPO2) measurement was recorded 15 minutes after electrode placement. The electrode was then removed and the machine was re-calibrated in preparation for a second recording. A carbon dioxide facial or microdermabrasion was then performed on the side of the face from which the baseline measurement was recorded. After treatment completion, the subject's cheek was wiped clean with dry gauze and again with alcohol and then allowed to dry. The electrode was re-positioned at the site of the initial recording. Following a 15-minute period to allow for equilibration, a final measurement of tcPO2 was documented.

FIGURE 1. OxyGeneoTM CO2 facial device comprised of interactive screen and handheld applicator with exfoliating capsule (Dermaspark Products Inc, Vancouver, British Columbia; Pollogen Ltd, Tel Aviv, Israel).

Once all data was collected, differences in tcPO2 before and after each treatment were calculated for each patient. The average tcPO2 difference following the carbon dioxide facial and the average tcPO2 difference after microdermabrasion were then generated for statistical analysis. Statistical significance was assessed by comparing the average tcPO2 difference (mmHg) following microdermabrasion and the average tcPO2 difference (mmHg) after the carbon dioxide facial using a 1-tailed paired t-test ($\alpha = 0.05$).

RESULTS

Though individual measurements varied by subject, the average value of tcPO2 at baseline was comparable prior to both procedures (Table 1). However, tcPO2 measurements taken 15 minutes after each treatment revealed that the average

TABLE 1.

	CO2 Facial (N = 12)	Microdermabrasion (N = 12)
Average tcPO2 at baseline (mmHg) +/- SEM	51.56 +/- 3.53	51.09 +/- 4.48
Average tcPO2 after treatment (mmHg) +/- SEM	62.85 +/- 2.64	57.06 +/- 4.13
Average tcPO2 difference (mmHg) +/- SEM	11.36 +/- 1.61*	5.97 +/- 1.10*

*P-value = 0.0252

increase in tcPO2 was greater following carbon dioxide facial therapy than after microdermabrasion (Table 1). To assess the statistical significance of these findings, a 1-tailed paired t-test ($\alpha = 0.05$) using values of ΔtcPO2 before and after each treatment was performed and yielded a P-value of 0.0252 (Table 2).

DISCUSSION

Carbon dioxide (CO2) therapy, known also as carboxytherapy, refers to the transcutaneous or subcutaneous administration of CO2 for therapeutic purposes[2]. Though originally engineered as a treatment for peripheral vascular disease, discovery of its aesthetic benefits over the past two decades has made it a growing topic in clinical research. In recent years, subcutaneous CO2 injections have shown promise in the localized treatment of fine lines and wrinkles, hyperpigmentation, localized adiposities, cellulite and facial scars.[3,8,9,10]

When first implemented in the treatment of peripheral vascular disease, the most commonly used carboxytherapy method involved direct application of CO2 by bathing the treatment area in either CO2-enriched water or natural CO2 spa gas.[11,12,13,14] Subcutaneous CO2 injections were gradually explored beginning in 1993, when pioneer research by Brandi et al demonstrated a significant increase in post-injection tcPO2 compared to baseline.[3]

The success of carboxytherapy in treating peripheral vascular disease is largely the result of CO2's effects on the microcirculation. CO2-mediated relaxation of smooth muscle promotes immediate vasodilation and increases delivery of oxygenated blood to tissue.[11,15,16,17,18] Increased perfusion also augments delivery of oxygen and nutrients and facilitates removal of unwanted waste products, such as free radicals.[20]

Long-term delivery of CO2 to the skin results in several benefits thought to result from permanent changes in circulatory parameters.[21] Prolonged CO2 excess promotes the release of growth factors that stimulate angiogenesis, a physiologic mechanism aimed at improving vascularization and delivery of oxygenated

TABLE 2.

Patient	Baseline tcPO2 before CO2 facial (mmHg)	TcPO2 after CO2 facial (mmHg)	ΔtcPO2	Baseline tcPO2 before microdermabrasion (mmHg)	TcPO2 after microdermabrasion (mmHg)	ΔtcPO2
1	61.9	70.5	8.6	43.7	45.2	1.5
2	44.9	54.5	9.6	30.2	43.3	13.1
3	55	69	14	77.6	78.8	1.2
4	32.3	58.1	25.8	56.3	58.7	2.4
5	62.6	73.8	11.2	50.2	60.4	10.2
6	52	57.3	5.3	62.4	69.3	6.9
7	41.2	56.2	15	38.3	49.1	10.8
8	44.5	54.4	9.9	29.3	34.1	4.8
9	71.1	76.2	5.1	54.1	56.9	2.8
10	66.2	74	7.8	62.4	68.7	6.3
11	36.2	50.4	14.2	38.5	43.7	5.2
12	50.2	59.8	9.8	70.1	76.5	6.4
	μ= 51.56 SEM = 3.53	μ = 62.85 SEM = 2.64	μ: 11.36* SEM = 1.61	μ = 51.09 SEM = 4.48	μ = 57.06 SEM = 4.13	μ: 5.97* SEM = 1.10

*P-value = 0.0252

blood to highly metabolic tissues.[18] Evidence for this effect was reported in a study by Irie et al that demonstrated induction of VEGF synthesis following carboxytherapy treatment in the form of a CO2-enriched water bath.[21] The release of angiogenic growth factors and the resulting expansion of the vascular supply improves tissue ability to acquire oxygen and nutrients necessary for optimal functioning.

Carboxytherapy has received even greater attention for its ability to oxygenate tissue, an effect stemming from the Bohr effect, a well-recognized physiologic process by which transportation of oxygen between tissues and the supplying circulation is regulated. When generated as a byproduct of metabolism in active tissues, CO2 diffuses into capillary blood and into red blood cells (RBCs). Within RBCs, carbonic anhydrase catalyzes a reaction between CO2 and water to generate carbonic acid, which quickly dissociates into protons and bicarbonate ions.[22] When bound to hemoglobin, these protons induce a conformational change that reduces hemoglobin's affinity for oxygen, thereby promoting the release of O2 to hypoxic tissues.[23] Oxygenation is further augmented by the release of vasodilatory compounds by RBCs, which sense hemoglobin's deoxygenated state and therefore O2 deficiency in surrounding tissue.[23]

Oxygen delivery is critical given its role in cellular respiration, where it is used for the production of adenosine triphosphates and other sources of biological energy needed to perform a wide array of cellular processes.[24] Specific investigation into the role of oxygen in the skin began in the 1960s, when Hunt et al. determined that oxygenation of wounds enhanced collagen synthesis and the formation of granulation tissue.[2,25] This made sense in light of later findings that the hydroxylation of proline and lysine, important steps in collagen synthesis, are dependent on oxygen, and was reinforced by the discovery that growth of tissue fibroblasts is related to oxygen tension.[6,26] These findings are supported by several recent studies specifically examining the ability of carboxytherapy to modulate the skin and subdermal layers. Ferrerira et al performed histologic analysis on skin samples from CO2-injected rats and reported a thicker dermis and more diffuse arrangement of collagen fibers compared to saline-treated controls.[7] It is this O2-mediated neocollagenesis that is believed to underlie improvements in skin elasticity and wrinkle reduction following subcutaneous CO2 injections.[8,19] In a similar vein, O2's ability to reorganize collagen is thought to explain the success of subcutaneous CO2 injections in the treatment of scar tissue.[10]

Despite this success, direct intradermal injections are invasive and carry several risks, including pain, bruising, swelling and infection.[3,8,15] Additionally, treatment of the entire face using this method is impractical. The carbon dioxide facial evaluated in this study is therefore unique in that it allows for non-invasive treatment of the entire face with very minimal side effects. The device is comprised of a handheld applicator, attached to which is a capsule composed of sodium bicarbonate and citric acid. This capsule interacts with one of two gels applied to the patient's face and generates a chemical reaction that produces CO2. Vibration of the applicator serves to exfoliate the stratum corneum and thereby reduce the foremost barrier to product penetration.

The purpose of our study was to assess the ability of the carbon dioxide facial to induce a Bohr effect and quantify the resulting oxygenation of tissue using measurements of transcutaneous oxygen tension (tcPO2). Unlike pulse oximeters that measure systemic O2 levels, tcPO2 is a local, non-invasive measurement that quantifies the amount of O2 that diffuses from capillaries and through the epidermis and has been shown to be a reliable measure of local skin oxygenation.[27]

Our data provides evidence for the ability of the CO2 facial to oxygenate tissue immediately after treatment. These findings are supported by a recently performed and comparable study that recorded tcPO2 before and after a CO2 facial and found a statistically significant increase independent of the anatomic area treated.[28] By comparing the average difference in tcPO2 following a CO2 facial to that following microdermabrasion, our study was also able to verify the Bohr effect as the mechanism by which oxygenation occurs. Determination that the average increase in tcPO2 following CO2 facial treatment was statistically significantly greater than following microdermabrasion allowed us to conclude that oxygenation of tissue following a CO2 facial is not attributed solely to exfoliation and a concomitant increase in blood flow. Rather, we believe that improvements in tissue oxygen were, like subcutaneous CO2 injections, largely the result of local application of CO2 and a rightward shift in the hemoglobin dissociation curve.

The results of this study offer preliminary evidence that the CO2 facial can effectively oxygenate the skin. However, further research is still required to demonstrate the clinical significance of this treatment. Whether the immediate increase in tissue oxygenation is the cause of any aesthetic improvements perceived after treatment is not yet clear. Furthermore, though our study demonstrates oxygenation immediately after the CO2 facial is more significant than exfoliation alone, it remains to be seen how long tissue oxygen levels remain elevated. One might expect that the longer tcPO2 remains elevated, the greater the visible skin improvement. A future trial comprised of a larger study population will also be necessary to strengthen the evidence presented. Future studies should also target the safety profile of this treatment, as it is still relatively novel and so its potential complications have not been thoroughly evaluated or proven with certainty. Though the low force generated during the CO2 facial aims to reduce the likelihood of complications, known side effects include temporary redness and discomfort ranging from mild tingling to moderate burning. Because of its

exfoliating properties, it is reasonable to ascertain that the CO2 facial may induce other undesirable side effects in susceptible patients, such as acne formation and hyperpigmentation. It is important to note, however, that none of our subjects reported these complications, nor did they experience any permanent or severe side effects. Nevertheless, the incidence of such complications is not clear and requires further evaluation as this treatment becomes more popular.

DISCLOSURES

The authors have no conflicts of interest to declare.

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